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(54) Title: <b>NOVEL MOLECULES OF THE TANGO-77 RELATED PROTEIN FAMILY AND USES THEREOF</b>				
(57) Abstract <p>Novel Tango-77 polypeptides, proteins, and nucleic acid molecules are disclosed. In addition to isolated, full-length Tango-77 proteins, the invention further provides isolated Tango-77 fusion proteins, antigenic peptides and anti-Tango-77 antibodies. The invention also provides Tango-77 nucleic acid molecules, recombinant expression vectors containing a nucleic acid molecule of the invention, host cells into which the expression vectors have been introduced and non-human transgenic animals in which a Tango-77 gene has been introduced or disrupted. Diagnostic, screening and therapeutic methods utilizing compositions of the invention are also provided.</p>				

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NOVEL MOLECULES OF THE TANGO-77 RELATED PROTEIN  
FAMILY AND USES THEREOF

Background of the Invention

The polypeptide cytokine interleukin-1 (IL-1) is a critical mediator of inflammatory and overall immune response. To date, three members of the IL-1 family, IL-1 $\alpha$ , IL-1 $\beta$  and IL-1ra (Interleukin-1 receptor antagonist) have been isolated and cloned. IL-1 $\alpha$  and IL-1 $\beta$  are proinflammatory cytokines which elicit biological responses, whereas IL-1ra is an antagonist of IL-1 $\alpha$  and IL-1 $\beta$  activity. Two distinct cell-surface receptors have been identified for these ligands, the type I IL-1 receptor (IL-1RtI) and type II IL-1 receptor (IL-1RtII). Recent results suggest that the IL-1RtI is the receptor responsible for transducing a signal and producing biological effects.

As mentioned above, IL-1 is a key mediator of the host inflammatory response. While inflammation is an important homeostatic mechanism, aberrant inflammation has the potential for inducing damage to the host. Elevated IL-1 levels are known to be associated with a number of diseases particularly autoimmune diseases and inflammatory disorders.

Since IL-1ra is a naturally occurring inhibitor of IL-1, IL-1ra can be used to limit the aberrant and potentially deleterious effects of IL-1. In experimental animals, pretreatment with IL-1ra has been shown to prevent death resulting from lipopolysaccharide-induced sepsis. The relative absence of IL-1ra has also been suggested to play a role in human inflammatory bowel disease.

Summary of the Invention

The present invention is based, at least in part, on the discovery of a gene encoding Tango-77, a secreted

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protein that is predicted to be a member of the cytokine superfamily. The Tango-77 cDNA described below (SEQ ID NO:1) has three possible open reading frames. The first potential open reading frame encompasses 534 nucleotides  
5 extending from nucleotide 356 to nucleotide 889 of SEQ ID NO:1 (SEQ ID NO:3) and encodes a 178 amino acid protein (SEQ ID NO:2). This protein may include a predicted signal sequence of about 63 amino acids (from about amino acid 1 to about amino acid 63 of SEQ ID NO:2 (SEQ ID  
10 NO:4) and a predicted mature protein of about 115 amino acids (from about amino acid 64 to amino acid 178 of SEQ ID NO:2 (SEQ ID NO:5)).

The second potential open reading frame encompasses 498 nucleotides extending from nucleotide 389  
15 to nucleotide 889 of SEQ ID NO:1 (SEQ ID NO:6) and encodes a 167 amino acid protein (SEQ ID NO:7). This protein may include a predicted signal sequence of about 52 amino acids (from about amino acid 1 to about amino acid 52 of SEQ ID NO:7 (SEQ ID NO:8)) and a predicted  
20 mature protein of about 115 amino acids (from about amino acid 52 to amino acid 167 of SEQ ID NO:7 (SEQ ID NO:9)).

The third potential open reading frame encompasses 408 nucleotides extending from nucleotide 481 to nucleotide 889 of SEQ ID NO:1 (SEQ ID NO:10) and encodes  
25 a 136 amino acid protein (SEQ ID NO:11). This protein includes a predicted signal sequence of about 21 amino acids (from about amino acid 1 to about amino acid 21 of SEQ ID NO:11 (SEQ ID NO:12)) and a predicted mature protein of about 115 amino acids (from about amino acid  
30 22 to amino acid 136 of SEQ ID NO:11 (SEQ ID NO:13)).

As used herein, the terms "Tango-77", "Tango-77 protein", "Tango-77 polypeptide" and the like, can refer and polypeptide produced by the cDNA of SEQ ID NO:1 including any and all of the Tango-77 gene products  
35 described above.



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Tango-77 is expected to inhibit inflammation and play a functional role similar to that of secreted IL-1ra. For example, it is expected that Tango-77 may bind to the IL-1 receptor, thus blocking receptor activation by inhibiting the binding of IL-1 $\alpha$  and IL-1 $\beta$  to the receptor. Alternatively, Tango-77 may inhibit inflammation through another pathway, for example, by binding to a novel receptor. Accordingly, Tango-77 may be useful as a modulating agent in regulating a variety of cellular processes including acute and chronic inflammation, e.g., asthma, chronic myelogenous leukemia, rheumatoid arthritis, psoriasis and inflammatory bowel disease.

In one aspect, the invention provides isolated nucleic acid molecules encoding Tango-77 or biologically active portions thereof, as well as nucleic acid fragments suitable as primers or hybridization probes for the detection of Tango-77.

The invention encompasses methods of diagnosing and treating patients who are suffering from a disorder associated with an abnormal level (undesirably high or undesirably low) of inflammation, abnormal activity of the IL-1 receptor complex, or abnormal activity of IL-1, by administering a compound that modulates the expression of Tango-77 (at the DNA, mRNA or protein level, e.g., by altering mRNA splicing) or by altering the activity of Tango-77. Examples of such compounds include small molecules, antisense nucleic acid molecules, ribozymes, and polypeptides.

The invention features a nucleic acid molecule which is at least 45% (e.g., 55%, 65%, 75%, 85%, 95%, or 98%) identical to the nucleotide sequence shown in SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the nucleotide sequence of the cDNA insert of the plasmid

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deposited with ATCC as Accession Number (the "cDNA of ATCC 98807"), or a complement thereof.

The invention features a nucleic acid molecule which includes a fragment of at least 100 (e.g., 250,  
5 325, 350, 375, 400, 425, 450, 500, 550, 600, 650, 700, 800, 900, or 989) nucleotides of the nucleotide sequence shown in SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the nucleotide sequence of the cDNA ATCC 98807, or a complement thereof.

10 The invention also features a nucleic acid molecule which includes a nucleotide sequence encoding a protein having an amino acid sequence that is at least 45% (55%, 65%, 75%, 85%, 95%, or 98%) identical to the amino acid sequence of SEQ ID NO:2, SEQ ID NO:5, SEQ ID  
15 NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, or the amino acid sequence encoded by the cDNA of ATCC 98807.

In a preferred embodiment, a Tango-77 nucleic acid molecule has the nucleotide sequence shown in SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10 or the  
20 nucleotide sequence of the cDNA of ATCC 98807.

Also within the invention is a nucleic acid molecule which encodes a fragment of a polypeptide having the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID  
25 NO:11, SEQ ID NO:12, SEQ ID NO:13, wherein the fragment includes at least 15 (e.g., 25, 30, 50, 100, 150, or 178) contiguous amino acids of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or the polypeptide  
30 encoded by the cDNA of ATCC Accession Number 98807.

The invention includes a nucleic acid molecule which encodes a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8,  
35 SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or

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an amino acid sequence encoded by the cDNA of ATCC Accession Number 98807, wherein the nucleic acid molecule hybridizes to a nucleic acid molecule comprising SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, or a complement thereof under stringent conditions.

Also within the invention are: an isolated Tango-77 protein having an amino acid sequence that is at least about 45%, preferably 65%, 75%, 85%, 95%, or 98% identical to the amino acid sequence of SEQ ID NO:5, SEQ ID NO:9 or SEQ ID NO:13 (mature human Tango-77), or the amino acid sequence of SEQ ID NO:2, SEQ ID NO:7 or SEQ ID NO:11 (immature human Tango-77).

Also within the invention are: an isolated Tango-77 protein which is encoded by a nucleic acid molecule having a nucleotide sequence that is at least about 65%, preferably 75%, 85%, or 95% identical to SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10 or the cDNA of ATCC 98807; and an isolated Tango-77 protein which is encoded by a nucleic acid molecule having a nucleotide sequence which hybridizes under stringent hybridization conditions to a nucleic acid molecule having the nucleotide sequence of SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the non-coding strand of the cDNA of ATCC 98807, or the complement thereof.

Also within the invention is a polypeptide which is a naturally occurring allelic variant of a polypeptide that includes the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or an amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807, wherein the polypeptide is encoded by a nucleic acid molecule which hybridizes to a nucleic acid molecule comprising SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID

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NO:10 or the complement thereof under stringent conditions.

Another embodiment of the invention features Tango-77 nucleic acid molecules which specifically detect  
5 Tango-77 nucleic acid molecules relative to nucleic acid molecules encoding other members of the cytokine superfamily. For example, in one embodiment, a Tango-77 nucleic acid molecule hybridizes under stringent conditions to a nucleic acid molecule comprising the  
10 nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the cDNA of ATCC 98807, or a complement thereof. In another embodiment, the Tango-77 nucleic acid molecule is at least 300 (325, 350, 375, 400, 425, 450, 500, 550, 600, 650, 700, 800, 900, or 989)  
15 nucleotides in length and hybridizes under stringent conditions to a nucleic acid molecule comprising the nucleotide sequence shown in SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the cDNA of ATCC 98807, or a complement thereof. In yet another embodiment, the  
20 invention provides an isolated nucleic acid molecule which is antisense to the coding strand of a Tango-77 nucleic acid.

Another aspect of the invention provides a vector, e.g., a recombinant expression vector, comprising a  
25 Tango-77 nucleic acid molecule of the invention. In another embodiment, the invention provides a host cell containing such a vector. The invention also provides a method for producing Tango-77 protein by culturing, in a suitable medium, a host cell of the invention containing  
30 a recombinant expression vector such that a Tango-77 protein is produced.

Another aspect of this invention features isolated or recombinant Tango-77 proteins and polypeptides. Preferred Tango-77 proteins and polypeptides possess at  
35 least one biological activity possessed by naturally

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occurring human Tango-77, e.g., (i) the ability to interact with proteins in the Tango-77 signalling pathway (ii) the ability to interact with a Tango-77 ligand or receptor; or (iii) the ability to interact with an intracellular target protein, (iv) the ability to  
5 interact with a protein involved in inflammation and (v) the ability to bind the IL-1 receptor. Other activities include the induction and suppression of polypeptide interleukins, cytokines and growth factors.

10 The Tango-77 proteins of the present invention, or biologically active portions thereof, can be operably linked to a non-Tango-77 polypeptide (e.g., heterologous amino acid sequences) to form Tango-77 fusion proteins. The invention further features antibodies that  
15 specifically bind Tango-77 proteins, such as monoclonal or polyclonal antibodies. In addition, the Tango-77 proteins or biologically active portions thereof can be incorporated into pharmaceutical compositions, which optionally include pharmaceutically acceptable carriers.

20 In another aspect, the present invention provides a method for detecting the presence of Tango-77 activity or expression in a biological sample by contacting the biological sample with an agent capable of detecting an indicator of Tango-77 activity or expression such that  
25 the presence of Tango-77 activity or expression is detected in the biological sample.

In another aspect, the invention provides a method for modulating Tango-77 activity comprising contacting a cell with an agent that modulates (inhibits or  
30 stimulates)

Tango-77 activity or expression such that Tango-77 activity or expression in the cell is modulated. In one embodiment, the agent is an antibody that specifically binds to Tango-77 protein. In another embodiment, the

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agent modulates expression of Tango-77 by modulating transcription of a Tango-77 gene, splicing of a Tango-77 mRNA, or translation of a Tango-77 mRNA. In yet another embodiment, the agent is a nucleic acid molecule having a  
5 nucleotide sequence that is antisense to the coding strand of the Tango-77 mRNA or the Tango-77 gene.

In one embodiment, the methods of the present invention are used to treat a subject having a disorder characterized by aberrant Tango-77 protein activity or  
10 nucleic acid expression by administering an agent which is a Tango-77 modulator to the subject. In one embodiment, the Tango-77 modulator is a Tango-77 protein. In another embodiment, the Tango-77 modulator is a Tango-77 nucleic acid molecule. In other embodiments,  
15 the Tango-77 modulator is a peptide, peptidomimetic, or other small molecule. In a preferred embodiment, the disorder characterized by aberrant Tango-77 protein or nucleic acid expression can include chronic and acute inflammation.

20 The present invention also provides a diagnostic assay for identifying the presence or absence of a genetic lesion or mutation characterized by at least one of: (i) aberrant modification or mutation of a gene encoding a Tango-77 protein; (ii) mis-regulation of a  
25 gene encoding a Tango-77 protein; and (iii) aberrant post-translational modification of a Tango-77 protein, wherein a wild-type form of the gene encodes a protein with a Tango-77 activity.

In another aspect, the invention provides a  
30 method for identifying a compound that binds to or modulates the activity of a Tango-77 protein. In general, such methods entail measuring a biological activity of a Tango-77 protein in the presence and absence of a test compound and identifying those

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compounds which alter the activity of the Tango-77 protein.

The invention also features methods for identifying a compound which modulates the expression of Tango-77 by measuring the expression of Tango-77 in the presence and absence of a compound.

Other features and advantages of the invention will be apparent from the following detailed description and claims.

#### Brief Description of the Drawings

Figure 1 depicts the cDNA sequence (SEQ ID NO:1) of Tango-77. The Tango-77 cDNA has three possible open reading frames which encode the amino acid sequence (SEQ ID NO:2, SEQ ID NO:7 and SEQ ID NO:11) of human Tango-77. The three potential open reading frames of SEQ ID NO:1 extend from: (1) nucleotide 356 to nucleotide 889 (SEQ ID NO:3); (2) nucleotide 389 to nucleotide 889 (SEQ ID NO:6); and (3) nucleotide 481 to nucleotide 889 (SEQ ID NO:10).

Figure 2 depicts an alignment of an amino acid sequence of Tango-77 (T77; SEQ ID NO:2) with IL-1RA (SEQ ID NO:14), and IL-1 $\beta$  (SEQ ID NO:15).

Figure 3 depicts the genomic sequence of BAC1 (SEQ ID NO:16).

Figure 4 depicts the genomic sequence of BAC2 (SEQ ID NO:17).

Figure 5 depicts an amino acid sequence of an alternatively spliced form of Tango-77 (SEQ ID NO:2) as predicted by Procrustes (T77-procrustes; SEQ ID NO:18).

Figure 6 depicts an alignment of an amino acid sequence of an alternatively spliced form of Tango-77 (T77-procrustes; SEQ ID NO:18) with Tango-77 (SEQ ID NO:2).

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Figure 7 depicts an alignment of an amino acid sequence of an alternatively spliced form of Tango-77 (T77-procrustes; SEQ ID NO:18) with IL-1ra (SEQ ID NO:14), and IL-1 $\beta$  (SEQ ID NO:15).

5                    Detailed Description of the Invention

The present invention is based on the discovery of a cDNA molecule encoding human Tango-77, a member of the cytokine superfamily. The cDNA molecule encoding human Tango-77 has three possible open reading frames. The  
10 three possible nucleotide open reading frames for human Tango-77 protein are shown in Figure 1 (SEQ ID NO:3, SEQ ID NO:6 and SEQ ID NO:10). The predicted amino acid sequence for the three possible Tango-77 immature proteins are also shown in  
15 Figure 1 (SEQ ID NO:2, SEQ ID NO:7 or SEQ ID NO:11) and three possible mature proteins are also shown in Figure 1 (SEQ ID NO:5, SEQ ID NO:9 and SEQ ID NO:13).

The Tango-77 cDNA of Figure 1 (SEQ ID NO:1), which is approximately 989 nucleotides long including  
20 untranslated regions, encodes a protein amino acid having a molecular weight of approximately 19 kDa, 18 kDa, or 14.9 kDa (excluding post-translational modifications) and the possible mature form of the protein has a molecular weight of 13 kDa. A plasmid containing a cDNA encoding  
25 human Tango-77 (with the cDNA insert name of Of fthx077) was deposited with American Type Culture Collection (ATCC), 10801 University Boulevard, Manassas, Virginia 20110-2209 on July 2, 1998 and assigned Accession Number 98807. This deposit will be maintained under the terms  
30 of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure. This deposit was made merely as a convenience for those of skill in the art and is not an



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admission that a deposit is required under 35 U.S.C. §112.

Human Tango-77 is one member of a family of molecules (the "Tango-77 family") having certain  
5 conserved structural and functional features. The term "family," when referring to the protein and nucleic acid molecules of the invention, is intended to mean two or more proteins or nucleic acid molecules having a common structural domain and having sufficient amino acid or  
10 nucleotide sequence identity as defined herein. Such family members can be naturally occurring and can be from either the same or different species. For example, a family can contain a first protein of human origin and a homologue of that protein of murine origin, as well as a  
15 second, distinct protein of human origin and a murine homologue of that protein. Members of a family may also have common functional characteristics.

As used interchangeably herein a "Tango-77 activity", "biological activity of Tango-77" or  
20 "functional activity of Tango-77", refers to an activity exerted by a Tango-77 protein, polypeptide or nucleic acid molecule on a Tango-77 responsive cell as determined *in vivo*, or *in vitro*, according to standard techniques. A Tango-77 activity can be a direct activity, such as an  
25 association with a second protein, or an indirect activity, such as a cellular signaling activity mediated by interaction of the Tango-77 protein with a second protein. In a preferred embodiment, a Tango-77 activity includes at least one or more of the following  
30 activities: (i) the ability to interact with proteins in the Tango-77 signalling pathway (ii) the ability to interact with a Tango-77 ligand or receptor; or (iii) the ability to interact with an intracellular target protein, (iv) the ability to interact with a protein involved in

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inflammation, and (v) the ability to bind the IL-1 receptor.

Accordingly, another embodiment of the invention features isolated Tango-77 proteins and polypeptides  
5 having a Tango-77 activity.

Yet another embodiment of the invention features Tango-77 molecules which contain a signal sequence. Generally, a signal sequence (or signal peptide) is a peptide containing about 21 to 63 amino acids which  
10 occurs at the extreme N-terminal end of a secretory protein. The native Tango-77 signal sequence (SEQ ID NO:4, SEQ ID NO:8, or SEQ ID NO:12) can be removed and replaced with a signal sequence from another protein. In certain host cells (e.g., mammalian host cells),  
15 expression and/or secretion of Tango-77 can be increased through use of a heterologous signal sequence. For example, the gp67 secretory sequence of the baculovirus envelope protein can be used as a heterologous signal sequence. Alternatively, the native Tango-77 signal  
20 sequence can itself be used as a heterologous signal sequence in expression systems, e.g., to facilitate the secretion of a protein of interest.

Various aspects of the invention are described in further detail in the following subsections.

25 I. Isolated Nucleic Acid Molecules

One aspect of the invention pertains to isolated nucleic acid molecules that encode Tango-77 proteins or biologically active portions thereof, as well as nucleic acid molecules sufficient for use as hybridization probes  
30 to identify Tango-77-encoding nucleic acids (e.g., Tango-77 mRNA) and fragments for use as PCR primers for the amplification or mutation of Tango-77 nucleic acid molecules. As used herein, the term "nucleic acid molecule" is intended to include DNA molecules (e.g.,

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cDNA or genomic DNA) and RNA molecules (e.g., mRNA) and analogs of the DNA or RNA generated using nucleotide analogs. The nucleic acid molecule can be single-stranded or double-stranded, but preferably is double-stranded DNA.

An "isolated" nucleic acid molecule is one which is separated from other nucleic acid molecules which are present in the natural source of the nucleic acid. Preferably, an "isolated" nucleic acid is free of sequences (preferably protein encoding sequences) which naturally flank the nucleic acid (i.e., sequences located at the 5' and 3' ends of the nucleic acid) in the genomic DNA of the organism from which the nucleic acid is derived. For example, in various embodiments, the isolated Tango-77 nucleic acid molecule can contain less than about 5 kb, 4 kb, 3 kb, 2 kb, 1 kb, 0.5 kb or 0.1 kb of nucleotide sequences which naturally flank the nucleic acid molecule in genomic DNA of the cell from which the nucleic acid is derived. Moreover, an "isolated" nucleic acid molecule, such as a cDNA molecule, can be substantially free of other cellular material, or culture medium when produced by recombinant techniques, or substantially free of chemical precursors or other chemicals when chemically synthesized.

A nucleic acid molecule of the present invention, e.g., a nucleic acid molecule having the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the cDNA of ATCC 98807, or a complement of any of these nucleotide sequences, can be isolated using standard molecular biology techniques and the sequence information provided herein. Using all or a portion of the nucleic acid sequences of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the cDNA of ATCC 98807, or the complement thereof as a hybridization probe, Tango-77 nucleic acid molecules can be isolated using standard

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hybridization and cloning techniques (e.g., as described in Sambrook et al., eds., *Molecular Cloning: A Laboratory Manual*, 2nd ed., Cold Spring Harbor Laboratory, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1989).

A nucleic acid of the invention can be amplified using cDNA, mRNA or genomic DNA as a template and appropriate oligonucleotide primers according to standard PCR amplification techniques. The nucleic acid so amplified can be cloned into an appropriate vector and characterized by DNA sequence analysis. Furthermore, oligonucleotides corresponding to Tango-77 nucleotide sequences can be prepared by standard synthetic techniques, e.g., using an automated DNA synthesizer.

In another preferred embodiment, an isolated nucleic acid molecule of the invention comprises a nucleic acid molecule which is a complement of the nucleotide sequence shown in SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10 the cDNA of ATCC 98807, or a portion thereof. A nucleic acid molecule which is complementary to a given nucleotide sequence is one which is sufficiently complementary to the given nucleotide sequence that it can hybridize to the given nucleotide sequence thereby forming a stable duplex.

Moreover, the nucleic acid molecule of the invention can comprise only a portion of a nucleic acid sequence encoding Tango-77, for example, a fragment which can be used as a probe or primer or a fragment encoding a biologically active portion of Tango-77. The nucleotide sequence determined from the cloning of the human Tango-77 gene allows for the generation of probes and primers designed for use in identifying and/or cloning Tango-77 homologues in other cell types, e.g., from other tissues, as well as Tango-77 homologues from other mammals. The probe/primer typically comprises

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substantially purified oligonucleotide. The oligonucleotide typically comprises a region of nucleotide sequence that hybridizes under stringent conditions to at least about 12, preferably about 25,  
5 more preferably about 50, 75, 100, 125, 150, 175, 200, 250, 300, 350 or 400 consecutive nucleotides of the sense or anti-sense sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, or the cDNA of ATCC 98807. Alternatively, the oligonucleotide can typically comprise  
10 a region of nucleotide sequence that hybridizes under stringent conditions to at least about 12, preferably about 25, more preferably about 50, 75, 100, 125, 150, 175, 200, 250, 300, 350 or 400 consecutive nucleotides of the sense or anti-sense sequence of a naturally occurring  
15 mutant of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, or the cDNA of ATCC 98807.

Probes based on the human Tango-77 nucleotide sequence can be used to detect transcripts or genomic sequences encoding the same or identical proteins. The  
20 probe comprises a label group attached thereto, e.g., a radioisotope, a fluorescent compound, an enzyme, or an enzyme co-factor. Such probes can be used as a part of a diagnostic test kit for identifying cells or tissues which mis-express a Tango-77 protein, such as by  
25 measuring a level of a Tango-77-encoding nucleic acid in a sample of cells from a subject, e.g., detecting Tango-77 mRNA levels or determining whether a genomic Tango-77 gene has been mutated or deleted.

A nucleic acid fragment encoding a "biologically  
30 active portion of Tango-77" can be prepared by isolating a portion of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10 or the nucleotide sequence of the cDNA of ATCC 98807 which encodes a polypeptide having a Tango-77 biological activity, expressing the encoded portion of  
35 Tango-77 protein (e.g., by recombinant expression in

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vitro) and assessing the activity of the encoded portion of Tango-77.

The invention further encompasses nucleic acid molecules that differ from the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, or the cDNA of ATCC 98807 due to degeneracy of the genetic code and thus encode the same Tango-77 protein as that encoded by the nucleotide sequence shown in SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, or the cDNA of ATCC 98807.

In addition to the human Tango-77 nucleotide sequence shown in SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, or the cDNA of ATCC 98807, it will be appreciated by those skilled in the art that DNA sequence polymorphisms that lead to changes in the amino acid sequences of Tango-77 may exist within a population (e.g., the human population). Such genetic polymorphism in the Tango-77 gene may exist among individuals within a population due to natural allelic variation. An allele is one of a group of genes which occur alternatively at a given genetic locus. As used herein, the term "allelic variant" refers to a nucleotide sequence which occurs at a Tango-77 locus or to a polypeptide encoded by the nucleotide sequence. As used herein, the terms "gene" and "recombinant gene" refer to nucleic acid molecules comprising an open reading frame encoding a Tango-77 protein, preferably a mammalian Tango-77 protein. Such natural allelic variations can typically result in 1-5% variance in the nucleotide sequence of the Tango-77 gene. Alternative alleles can be identified by sequencing the gene of interest in a number of different individuals. This can be readily carried out by using hybridization probes to identify the same genetic locus in a variety of individuals. Any and all such nucleotide variations and resulting amino acid polymorphisms or variations in

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Tango-77 that are the result of natural allelic variation and that do not alter the functional activity of Tango-77 are intended to be within the scope of the invention.

Moreover, nucleic acid molecules encoding Tango-77  
5 proteins from other species (Tango-77 homologues), which have a nucleotide sequence which differs from that of a human Tango-77, are intended to be within the scope of the invention. Nucleic acid molecules corresponding to natural allelic variants and homologues of the Tango-77  
10 cDNA of the invention can be isolated based on their identity to the human Tango-77 nucleic acids disclosed herein using the human cDNAs, or a portion thereof, as a hybridization probe according to standard hybridization techniques under stringent hybridization conditions.

15 Accordingly, in another embodiment, an isolated nucleic acid molecule of the invention is at least 300 (325, 350, 375, 400, 425, 450, 500, 550, 600, 650, 700, 800, or 989) nucleotides in length and hybridizes under stringent conditions to the nucleic acid molecule  
20 comprising the nucleotide sequence, preferably the coding sequence, of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, or the cDNA of ATCC 98807.

As used herein, the term "hybridizes under stringent conditions" is intended to describe conditions  
25 for hybridization and washing under which nucleotide sequences at least 60% (65%, 70%, preferably 75%) identical to each other typically remain hybridized to each other. Such stringent conditions are known to those skilled in the art and can be found in *Current Protocols*  
30 in *Molecular Biology*, John Wiley & Sons, N.Y. (1989), 6.3.1-6.3.6. A preferred, non-limiting example of stringent hybridization conditions are hybridization in 6X sodium chloride/sodium citrate (SSC) at about 45°C, followed by one or more washes in 0.2X SSC, 0.1% SDS at  
35 50-65°C. Preferably, an isolated nucleic acid molecule

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of the invention that hybridizes under stringent conditions to the sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the cDNA of ATCC 98807, or the complement thereof, corresponds to a naturally-occurring  
5 nucleic acid molecule. As used herein, a "naturally-occurring" nucleic acid molecule refers to an RNA or DNA molecule having a nucleotide sequence that occurs in nature (e.g., encodes a natural protein).

In addition to naturally-occurring allelic  
10 variants of the Tango-77 sequence that may exist in the population, the skilled artisan will further appreciate that changes can be introduced by mutation into the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10 or the cDNA of ATCC 98807, thereby  
15 leading to changes in the amino acid sequence of the encoded Tango-77 protein, without altering the biological activity of the Tango-77 protein. Amino acid residues that are not conserved or only semiconserved among Tango-77 of various species may be non-essential for activity  
20 and thus would likely be targets for alteration. Alternatively, one can make nucleotide substitutions leading to amino acid substitutions at "non-essential" amino acid residues. A "non-essential" amino acid residue is a residue that can be altered from the wild-  
25 type sequence of Tango-77 (e.g., the sequence of SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11 or SEQ ID NO:13) without altering the biological activity, whereas an "essential" amino acid residue is required for biological activity. For example, amino  
30 acid residues that are conserved among the Tango-77 proteins of various species may be essential for activity and thus would not likely be targets for alteration, unless one wishes to reduce or alter Tango-77 activity.

Accordingly, another aspect of the invention  
35 pertains to nucleic acid molecules encoding Tango-77



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proteins that contain changes in amino acid residues that are not essential for activity. Such Tango-77 proteins differ in amino acid sequence from SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13 yet retain biological activity. In one embodiment, the isolated nucleic acid molecule includes a nucleotide sequence encoding a protein that includes an amino acid sequence that is at least about 45% identical, 65%, 75%, 85%, 95%, or 98% identical to the amino acid sequence of SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13.

An isolated nucleic acid molecule encoding a Tango-77 protein having a sequence which differs from that of SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13 can be created by introducing one or more nucleotide substitutions, additions or deletions into the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, or the cDNA of ATCC 98807 such that one or more amino acid substitutions, additions or deletions are introduced into the encoded protein. Mutations can be introduced by standard techniques, such as site-directed mutagenesis and PCR-mediated mutagenesis. Preferably, conservative amino acid substitutions are made at one or more predicted non-essential amino acid residues. A "conservative amino acid substitution" is one in which the amino acid residue is replaced with an amino acid residue having a similar side chain. Families of amino acid residues having similar side chains have been defined in the art. These families include amino acids with basic side chains (e.g., lysine, arginine, histidine), acidic side chains (e.g., aspartic acid, glutamic acid), uncharged polar side chains (e.g., glycine, asparagine, glutamine, serine, threonine, tyrosine, cysteine), nonpolar side chains (e.g., alanine,

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valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan), beta-branched side chains (e.g., threonine, valine, isoleucine) and aromatic side chains (e.g., tyrosine, phenylalanine, tryptophan, histidine).

5 Thus, a predicted nonessential amino acid residue in Tango-77 is preferably replaced with another amino acid residue from the same side chain family. Alternatively, mutations can be introduced randomly along all or part of a Tango-77 coding sequence, such as by saturation  
10 mutagenesis, and the resultant mutants can be screened for Tango-77 biological activity to identify mutants that retain activity. Following mutagenesis, the encoded protein can be expressed recombinantly and the activity of the protein can be determined.

15 In a preferred embodiment, a mutant Tango-77 protein can be assayed for: (1) the ability to form protein:protein interactions with proteins in the Tango-77 signalling pathway; (2) the ability to bind a Tango-77 ligand or receptor; or (3) the ability to bind  
20 to an intracellular target protein or (4) the ability to interact with a protein involved in inflammation or (5) the ability to bind the IL-1 receptor. In yet another preferred embodiment, a mutant Tango-77 can be assayed for the ability to modulate inflammation, asthma,  
25 autoimmune diseases, and sepsis.

The present invention encompasses antisense nucleic acid molecules, i.e., molecules which are complementary to a sense nucleic acid encoding a protein, e.g., complementary to the coding strand of a double-  
30 stranded cDNA molecule or complementary to an mRNA sequence. Accordingly, an antisense nucleic acid can hydrogen bond to a sense nucleic acid. The antisense nucleic acid can be complementary to an entire Tango-77 coding strand, or to only a portion thereof, e.g., all or  
35 part of the protein coding region (or open reading

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frame). An antisense nucleic acid molecule can be antisense to a noncoding region of the coding strand of a nucleotide sequence encoding Tango-77. The noncoding regions ("5' and 3' untranslated regions") are the 5' and 3' sequences which flank the coding region and are not translated into amino acids.

Given the coding strand sequences encoding Tango-77 disclosed herein (e.g., SEQ ID NO:3, SEQ ID NO:5, or SEQ ID NO:8), antisense nucleic acids of the invention can be designed according to the rules of Watson and Crick base pairing. The antisense nucleic acid molecule can be complementary to the entire coding region of Tango-77 mRNA, but more preferably is an oligonucleotide which is antisense to only a portion of the coding or noncoding region of Tango-77 mRNA. For example, the antisense oligonucleotide can be complementary to the region surrounding the translation start site of Tango-77 mRNA, e.g., an oligonucleotide having the sequence 5'-TGCAACTTTTACAGGAAACAC-3' (SEQ ID NO:19) or 5'-CCTCACTTTTACCCGAGACTC-3' (SEQ ID NO:20) or 5'-GACGGGTGGTACTTAAACAA-3' (SEQ ID NO:21). An antisense oligonucleotide can be, for example, about 5, 10, 15, 20, 25, 30, 35, 40, 45 or 50 nucleotides in length. An antisense nucleic acid of the invention can be constructed using chemical synthesis and enzymatic ligation reactions using procedures known in the art. For example, an antisense nucleic acid (e.g., an antisense oligonucleotide) can be chemically synthesized using naturally occurring nucleotides or variously modified nucleotides designed to increase the biological stability of the molecules or to increase the physical stability of the duplex formed between the antisense and sense nucleic acids, e.g., phosphorothioate derivatives and acridine substituted nucleotides can be used. Examples of modified nucleotides which can be used to

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generate the antisense nucleic acid include 5-fluorouracil, 5-bromouracil, 5-chlorouracil, 5-iodouracil, hypoxanthine, xanthine, 4-acetylcytosine, 5-(carboxyhydroxymethyl) uracil, 5-carboxymethylaminomethyl-2-thiouridine, 5-carboxymethylaminomethyluracil, dihydrouracil, beta-D-galactosylqueosine, inosine, N6-isopentenyladenine, 1-methylguanine, 1-methylinosine, 2,2-dimethylguanine, 2-methyladenine, 2-methylguanine, 3-methylcytosine, 5-methylcytosine, N6-adenine, 7-methylguanine, 5-methylaminomethyluracil, 5-methoxyaminomethyl-2-thiouracil, beta-D-mannosylqueosine, 5'-methoxycarboxymethyluracil, 5-methoxyuracil, 2-methylthio-N6-isopentenyladenine, uracil-5-oxyacetic acid (v), wybutoxosine, pseudouracil, queosine, 2-thiocytosine, 5-methyl-2-thiouracil, 2-thiouracil, 4-thiouracil, 5-methyluracil, uracil-5-oxyacetic acid methylester, uracil-5-oxyacetic acid (v), 5-methyl-2-thiouracil, 3-(3-amino-3-N-2-carboxypropyl) uracil (acp3)w, and 2,6-diaminopurine. Alternatively, the antisense nucleic acid can be produced biologically using an expression vector into which a nucleic acid has been subcloned in an antisense orientation (i.e., RNA transcribed from the inserted nucleic acid will be of an antisense orientation to a target nucleic acid of interest, described further in the following subsection).

The antisense nucleic acid molecules of the invention are typically administered to a subject or generated *in situ* such that they hybridize with or bind to cellular mRNA and/or genomic DNA encoding a Tango-77 protein to thereby inhibit expression of the protein, e.g., by inhibiting transcription and/or translation. The hybridization can be by conventional nucleotide complementarity to form a stable duplex, or, for example, in the case of an antisense nucleic acid molecule which

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binds to DNA duplexes, through specific interactions in the major groove of the double helix. An example of a route of administration of antisense nucleic acid molecules of the invention includes direct injection at a tissue site. Alternatively, antisense nucleic acid molecules can be modified to target selected cells and then administered systemically. For example, for systemic administration, antisense molecules can be modified such that they specifically bind to receptors or antigens expressed on a selected cell surface, e.g., by linking the antisense nucleic acid molecules to peptides or antibodies which bind to cell surface receptors or antigens. The antisense nucleic acid molecules can also be delivered to cells using the vectors described herein. To achieve sufficient intracellular concentrations of the antisense molecules, vector constructs in which the antisense nucleic acid molecule is placed under the control of a strong pol II or pol III promoter are preferred.

An antisense nucleic acid molecule of the invention can be an  $\alpha$ -anomeric nucleic acid molecule. An  $\alpha$ -anomeric nucleic acid molecule forms specific double-stranded hybrids with complementary RNA in which, contrary to the usual  $\beta$ -units, the strands run parallel to each other (Gaultier et al. (1987) *Nucleic Acids Res.* 15:6625-6641). The antisense nucleic acid molecule can also comprise a 2'-O-methylribonucleotide (Inoue et al. (1987) *Nucleic Acids Res.* 15:6131-6148) or a chimeric RNA-DNA analogue (Inoue et al. (1987) *FEBS Lett.* 215:327-330).

The invention also encompasses ribozymes. Ribozymes are catalytic RNA molecules with ribonuclease activity which are capable of cleaving a single-stranded nucleic acid, such as an mRNA, to which they have a complementary region. Thus, ribozymes (e.g., hammerhead

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ribozymes (described in Haselhoff and Gerlach (1988) Nature 334:585-591)) can be used to catalytically cleave Tango-77 mRNA transcripts to thereby inhibit translation of Tango-77 mRNA. A ribozyme having specificity for a  
5 Tango-77-encoding nucleic acid can be designed based upon the nucleotide sequence of a Tango-77 cDNA disclosed herein (e.g., SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10). For example, a derivative of a Tetrahymena L-19 IVS RNA can be constructed in which the nucleotide  
10 sequence of the active site is complementary to the nucleotide sequence to be cleaved in a Tango-77-encoding mRNA. See, e.g., Cech et al. U.S. Patent No. 4,987,071; and Cech et al. U.S. Patent No. 5,116,742. Alternatively, Tango-77 mRNA can be used to select a  
15 catalytic RNA having a specific ribonuclease activity from a pool of RNA molecules. See, e.g., Bartel and Szostak (1993) Science 261:1411-1418.

The invention also encompasses nucleic acid molecules which form triple helical structures. For  
20 example, Tango-77 gene expression can be inhibited by targeting nucleotide sequences complementary to the regulatory region of the Tango-77 (e.g., the Tango-77 promoter and/or enhancers) to form triple helical structures that prevent transcription of the Tango-77  
25 gene in target cells. See generally, Helene (1991) Anticancer Drug Des. 6(6):569-84; Helene (1992) Ann. N.Y. Acad. Sci. 660:27-36; and Maher (1992) Bioassays 14(12):807-15.

In preferred embodiments, the nucleic acid  
30 molecules of the invention can be modified at the base moiety, sugar moiety or phosphate backbone to improve, e.g., the stability, hybridization, or solubility of the molecule. For example, the deoxyribose phosphate backbone of the nucleic acids can be modified to generate  
35 peptide nucleic acids (see Hyrup et al. (1996) Bioorganic

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& *Medicinal Chemistry* 4(1): 5-23). As used herein, the terms "peptide nucleic acids" or "PNAs" refer to nucleic acid mimics, e.g., DNA mimics, in which the deoxyribose phosphate backbone is replaced by a pseudopeptide backbone and only the four natural nucleobases are retained. The neutral backbone of PNAs has been shown to allow for specific hybridization to DNA and RNA under conditions of low ionic strength. The synthesis of PNA oligomers can be performed using standard solid phase peptide synthesis protocols as described in Hyrup et al. (1996) *supra*; Perry-O'Keefe et al. (1996) *Proc. Natl. Acad. Sci. USA* 93: 14670-675.

PNAs of Tango-77 can be used in therapeutic and diagnostic applications. For example, PNAs can be used as antisense or antigene agents for sequence-specific modulation of gene expression by, e.g., inducing transcription or translation arrest or inhibiting replication. PNAs of Tango-77 can also be used, e.g., in the analysis of single base pair mutations in a gene by, e.g., PNA directed PCR clamping; as artificial restriction enzymes when used in combination with other enzymes, e.g., S1 nucleases (Hyrup (1996) *supra*; or as probes or primers for DNA sequence and hybridization (Hyrup (1996) *supra*; Perry-O'Keefe et al. (1996) *Proc. Natl. Acad. Sci. USA* 93: 14670-675).

In another embodiment, PNAs of Tango-77 can be modified, e.g., to enhance their stability or cellular uptake, by attaching lipophilic or other helper groups to PNA, by the formation of PNA-DNA chimeras, or by the use of liposomes or other techniques of drug delivery known in the art. For example, PNA-DNA chimeras of Tango-77 can be generated which may combine the advantageous properties of PNA and DNA. Such chimeras allow DNA recognition enzymes, e.g., RNase H and DNA polymerases, to interact with the DNA portion while the PNA portion

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would provide high binding affinity and specificity. PNA-DNA chimeras can be linked using linkers of appropriate lengths selected in terms of base stacking, number of bonds between the nucleobases, and orientation (Hyrup (1996) *supra*). The synthesis of PNA-DNA chimeras can be performed as described in Hyrup (1996) *supra* and Finn et al. (1996) *Nucleic Acids Res.* 24(17):3357-63. For example, a DNA chain can be synthesized on a solid support using standard phosphoramidite coupling chemistry and modified nucleoside analogs. Compounds such as 5'-(4-methoxytrityl)amino-5'-deoxy-thymidine phosphoramidite can be used as a link between the PNA and the 5' end of DNA (Mag et al. (1989) *Nucleic Acid Res.* 17:5973-88). PNA monomers are then coupled in a stepwise manner to produce a chimeric molecule with a 5' PNA segment and a 3' DNA segment (Finn et al. (1996) *Nucleic Acids Res.* 24(17):3357-63). Alternatively, chimeric molecules can be synthesized with a 5' DNA segment and a 3' PNA segment (Peterser et al. (1975) *Bioorganic Med. Chem. Lett.* 5:1119-11124).

In other embodiments, the oligonucleotide may include other appended groups such as peptides (e.g., for targeting host cell receptors *in vivo*), or agents facilitating transport across the cell membrane (see, e.g., Letsinger et al. (1989) *Proc. Natl. Acad. Sci. USA* 86:6553-6556; Lemaitre et al. (1987) *Proc. Natl. Acad. Sci. USA* 84:648-652; PCT Publication No. WO 88/09810) or the blood-brain barrier (see, e.g., PCT Publication No. WO 89/10134). In addition, oligonucleotides can be modified with hybridization-triggered cleavage agents (see, e.g., Krol et al. (1988) *Bio/Techniques* 6:958-976) or intercalating agents (see, e.g., Zon (1988) *Pharm. Res.* 5:539-549). To this end, the oligonucleotide may be conjugated to another molecule, e.g., a peptide,



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hybridization triggered cross-linking agent, transport agent, hybridization-triggered cleavage agent, etc.

## II. Isolated Tango-77 Proteins and Anti-Tango-77 Antibodies

5 One aspect of the invention pertains to isolated Tango-77 proteins, and biologically active portions thereof, as well as polypeptide fragments suitable for use as immunogens to raise anti-Tango-77 antibodies. In one embodiment, native Tango-77 proteins can be isolated  
10 from cells or tissue sources by an appropriate purification scheme using standard protein purification techniques. In another embodiment, Tango-77 proteins are produced by recombinant DNA techniques. Alternative to recombinant expression, a Tango-77 protein or polypeptide  
15 can be synthesized chemically using standard peptide synthesis techniques.

An "isolated" or "purified" protein or biologically active portion thereof is substantially free of cellular material or other contaminating proteins from  
20 the cell or tissue source from which the Tango-77 protein is derived, or substantially free of chemical precursors or other chemicals when chemically synthesized. The language "substantially free of cellular material" includes preparations of Tango-77 protein in which the  
25 protein is separated from cellular components of the cells from which it is isolated or recombinantly produced. Thus, Tango-77 protein that is substantially free of cellular material includes preparations of Tango-77 protein having less than about 30%, 20%, 10%, or  
30 5% (by dry weight) of non-Tango-77 protein (also referred to herein as a "contaminating protein"). When the Tango-77 protein or biologically active portion thereof is recombinantly produced, it is also preferably substantially free of culture medium, i.e., culture

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medium represents less than about 20%, 10%, or 5% of the volume of the protein preparation. When Tango-77 protein is produced by chemical synthesis, it is preferably substantially free of chemical precursors or other chemicals, i.e., it is separated from chemical precursors or other chemicals which are involved in the synthesis of the protein. Accordingly such preparations of Tango-77 protein have less than about 30%, 20%, 10%, 5% (by dry weight) of chemical precursors or non-Tango-77 chemicals.

Biologically active portions of a Tango-77 protein include peptides comprising amino acid sequences sufficiently identical to or derived from the amino acid sequence of the Tango-77 protein (e.g., the amino acid sequence shown in SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13), which include fewer amino acids than the full length Tango-77 proteins, and exhibit at least one activity of a Tango-77 protein. Typically, biologically active portions comprise a domain or motif with at least one activity of the Tango-77 protein. A biologically active portion of a Tango-77 protein can be a polypeptide which is, for example, 10, 25, 50, 100 or more amino acids in length.

Moreover, other biologically active portions, in which other regions of the protein are deleted, can be prepared by recombinant techniques and evaluated for one or more of the functional activities of a native Tango-77 protein.

Preferred Tango-77 protein has the amino acid sequence shown of SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13. Other useful Tango-77 proteins are substantially identical to SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13 and retain the functional activity of the protein of SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13 yet differ in

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amino acid sequence due to natural allelic variation or mutagenesis. Accordingly, a useful Tango-77 protein is a protein which includes an amino acid sequence at least about 45%, preferably 55%, 65%, 75%, 85%, 95%, or 99% identical to the amino acid sequence of SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13 and retains the functional activity of the Tango-77 proteins of SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13. In a preferred embodiment, the Tango-77 protein retains a functional activity of the Tango-77 protein of SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13.

To determine the percent identity of two amino acid sequences or of two nucleic acids, the sequences are aligned for optimal comparison purposes (e.g., gaps can be introduced in the sequence of a first amino acid or nucleic acid sequence for optimal alignment with a second amino or nucleic acid sequence). The amino acid residues or nucleotides at corresponding amino acid positions or nucleotide positions are then compared. When a position in the first sequence is occupied by the same amino acid residue or nucleotide as the corresponding position in the second sequence, then the molecules are identical at that position. The percent identity between the two sequences is a function of the number of identical positions shared by the sequences (i.e., % identity = # of identical positions/total # of positions, e.g., overlapping x 100). Preferably, the two sequences are the same length.

The determination of percent homology between two sequences can be accomplished using a mathematical algorithm. A preferred, non-limiting example of a mathematical algorithm utilized for the comparison of two sequences is the algorithm of Karlin and Altschul (1990)

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Proc. Natl. Acad. Sci. USA 87:2264-2268, modified as in Karlin and Altschul (1993) Proc. Natl. Acad. Sci. USA 90:5873-5877. Such an algorithm is incorporated into the NBLAST and XBLAST programs of Altschul, et al. (1990) J. Mol. Biol. 215:403-410. BLAST nucleotide searches can be performed with the NBLAST program, score = 100, wordlength = 12 to obtain nucleotide sequences homologous to Tango-77 nucleic acid molecules of the invention. BLAST protein searches can be performed with the XBLAST program, score = 50, wordlength = 3 to obtain amino acid sequences homologous to Tango-77 protein molecules of the invention. To obtain gapped alignments for comparison purposes, Gapped BLAST can be utilized as described in Altschul et al. (1997) Nucleic Acids Res. 25:3389-3402. When utilizing BLAST and Gapped BLAST programs, the default parameters of the respective programs (e.g., XBLAST and NBLAST) can be used. See <http://www.ncbi.nlm.nih.gov>. Another preferred, non-limiting example of a mathematical algorithm utilized for the comparison of sequences is the algorithm of Myers and Miller, CABIOS (1989). Such an algorithm is incorporated into the ALIGN program (version 2.0) which is part of the GCG sequence alignment software package. When utilizing the ALIGN program for comparing amino acid sequences, a PAM120 weight residue table, a gap length penalty of 12, and a gap penalty of 4 can be used.

The percent identity between two sequences can be determined using techniques similar to those described above, with or without allowing gaps. In calculating percent identity, only exact matches are counted.

The invention also provides Tango-77 chimeric or fusion proteins. As used herein, a Tango-77 "chimeric protein" or "fusion protein" comprises a Tango-77 polypeptide operably linked to a non-Tango-77 polypeptide. A "Tango-77 polypeptide" refers to a

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polypeptide having an amino acid sequence corresponding to Tango-77 polypeptides, whereas a "non-Tango-77 polypeptide" refers to a polypeptide having an amino acid sequence corresponding to a protein which is not substantially identical to the Tango-77 protein, e.g., a protein which is different from the Tango-77 protein and which is derived from the same or a different organism. Within a Tango-77 fusion protein the Tango-77 polypeptide can correspond to all or a portion of a Tango-77 protein, preferably at least one biologically active portion of a Tango-77 protein. Within the fusion protein, the term "operably linked" is intended to indicate that the Tango-77 polypeptide and the non-Tango-77 polypeptide are fused in-frame to each other. The non-Tango-77 polypeptide can be fused to the N-terminus or C-terminus of the Tango-77 polypeptide.

One useful fusion protein is a GST-Tango-77 fusion protein in which the Tango-77 sequences are fused to the C-terminus of the GST sequences. Such fusion proteins can facilitate the purification of recombinant Tango-77.

In another embodiment, the fusion protein is a Tango-77 protein containing a heterologous signal sequence at its N-terminus. For example, the native Tango-77 signal sequence (i.e., about amino acids 1 to 63 of SEQ ID NO:2; SEQ ID NO:4; or about amino acids 1 to 52 of SEQ ID NO:7; SEQ ID NO:8; or about amino acids 1 to 21 of SEQ ID NO:11; SEQ ID NO:12) can be removed and replaced with a signal sequence from another protein. In certain host cells (e.g., mammalian host cells), expression and/or secretion of Tango-77 can be increased through use of a heterologous signal sequence. For example, the gp67 secretory sequence of the baculovirus envelope protein can be used as a heterologous signal sequence (Ausubel et al., supra). Other examples of eukaryotic heterologous signal sequences include the secretory sequences of

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melittin and human placental alkaline phosphatase (Stratagene; La Jolla, California). In yet another example, useful prokaryotic heterologous signal sequences include the phoA secretory signal (Sambrook et al.,  
5 supra) and the protein A secretory signal (Pharmacia Biotech; Piscataway, New Jersey).

In yet another embodiment, the fusion protein is an Tango-77-immunoglobulin fusion protein in which all or part of Tango-77 is fused to sequences derived from a  
10 member of the immunoglobulin protein family. The Tango-77-immunoglobulin fusion proteins of the invention can be incorporated into pharmaceutical compositions and administered to a subject to inhibit an interaction  
15 between a Tango-77 ligand and a Tango-77 receptor on the surface of a cell, to thereby suppress Tango-77-mediated signal transduction in vivo. The Tango-77-immunoglobulin fusion proteins can be used to affect the bioavailability of a Tango-77 cognate ligand. Inhibition of the Tango-77  
20 ligand/Tango-77 interaction may be useful therapeutically for both the treatment of inflammatory and autoimmune disorders. Moreover, the Tango-77-immunoglobulin fusion proteins of the invention can be used as immunogens to produce anti-Tango-77 antibodies in a subject, to purify  
25 Tango-77 ligands and in screening assays to identify molecules which inhibit the interaction of Tango-77 with a Tango-77 receptor.

Preferably, a Tango-77 chimeric or fusion protein of the invention is produced by standard recombinant DNA techniques. For example, DNA fragments coding for the  
30 different polypeptide sequences are ligated together in-frame in accordance with conventional techniques, for example by employing blunt-ended or stagger-ended termini for ligation, restriction enzyme digestion to provide for appropriate termini, filling-in of cohesive ends as  
35 appropriate, alkaline phosphatase treatment to avoid

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undesirable joining, and enzymatic ligation. In another embodiment, the fusion gene can be synthesized by conventional techniques including automated DNA synthesizers. Alternatively, PCR amplification of gene fragments can be carried out using anchor primers which give rise to complementary overhangs between two consecutive gene fragments which can subsequently be annealed and reamplified to generate a chimeric gene sequence (see, e.g., *Current Protocols in Molecular Biology*, Ausubel et al. eds., John Wiley & Sons: 1992). Moreover, many expression vectors are commercially available that already encode a fusion moiety (e.g., a GST polypeptide). An Tango-77-encoding nucleic acid can be cloned into such an expression vector such that the fusion moiety is linked in-frame to the Tango-77 protein.

The present invention also pertains to variants of the Tango-77 proteins (i.e., proteins having a sequence which differs from that of the Tango-77 amino acid sequence). Such variants can function as either Tango-77 agonists (mimetics) or as Tango-77 antagonists. Variants of the Tango-77 protein can be generated by mutagenesis, e.g., discrete point mutation or truncation of the Tango-77 protein. An agonist of the Tango-77 protein can retain substantially the same, or a subset, of the biological activities of the naturally occurring form of the Tango-77 protein. An antagonist of the Tango-77 protein can inhibit one or more of the activities of the naturally occurring form of the Tango-77 protein by, for example, competitively binding to a downstream or upstream member of a cellular signaling cascade which includes the Tango-77 protein. Thus, specific biological effects can be elicited by treatment with a variant of limited function. Treatment of a subject with a variant having a subset of the biological activities of the naturally occurring form of the protein can have fewer

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side effects in a subject relative to treatment with the naturally occurring form of the Tango-77 proteins.

Variants of the Tango-77 protein which function as either Tango-77 agonists (mimetics) or as Tango-77  
5 antagonists can be identified by screening combinatorial libraries of mutants, e.g., truncation mutants, of the Tango-77 protein for Tango-77 protein agonist or antagonist activity. In one embodiment, a variegated library of Tango-77 variants is generated by  
10 combinatorial mutagenesis at the nucleic acid level and is encoded by a variegated gene library. A variegated library of Tango-77 variants can be produced by, for example, enzymatically ligating a mixture of synthetic oligonucleotides into gene sequences such that a  
15 degenerate set of potential Tango-77 sequences is expressible as individual polypeptides, or alternatively, as a set of larger fusion proteins (e.g., for phage display) containing the set of Tango-77 sequences therein. There are a variety of methods which can be  
20 used to produce libraries of potential Tango-77 variants from a degenerate oligonucleotide sequence. Chemical synthesis of a degenerate gene sequence can be performed in an automatic DNA synthesizer, and the synthetic gene then ligated into an appropriate expression vector. Use  
25 of a degenerate set of genes allows for the provision, in one mixture, of all of the sequences encoding the desired set of potential Tango-77 sequences. Methods for synthesizing degenerate oligonucleotides are known in the art (see, e.g., Narang (1983) *Tetrahedron* 39:3; Itakura  
30 et al. (1984) *Annu. Rev. Biochem.* 53:323; Itakura et al. (1984) *Science* 198:1056; Ike et al. (1983) *Nucleic Acid Res.* 11:477).

In addition, libraries of fragments of the Tango-77 protein coding sequence can be used to generate  
35 a variegated population of Tango-77 fragments for



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screening and subsequent selection of variants of a Tango-77 protein. In one embodiment, a library of coding sequence fragments can be generated by treating a double stranded PCR fragment of a Tango-77 coding sequence with  
5 a nuclease under conditions wherein nicking occurs only about once per molecule, denaturing the double stranded DNA, renaturing the DNA to form double stranded DNA which can include sense/antisense pairs from different nicked products, removing single stranded portions from reformed  
10 duplexes by treatment with S1 nuclease, and ligating the resulting fragment library into an expression vector. By this method, an expression library can be derived which encodes N-terminal and internal fragments of various sizes of the Tango-77 protein.

15 Several techniques are known in the art for screening gene products of combinatorial libraries made by point mutations or truncation, and for screening cDNA libraries for gene products having a selected property. Such techniques are adaptable for rapid screening of the  
20 gene libraries generated by the combinatorial mutagenesis of Tango-77 proteins. The most widely used techniques, which are amenable to high through-put analysis, for screening large gene libraries typically include cloning the gene library into replicable expression vectors,  
25 transforming appropriate cells with the resulting library of vectors, and expressing the combinatorial genes under conditions in which detection of a desired activity facilitates isolation of the vector encoding the gene whose product was detected. Recursive ensemble  
30 mutagenesis (REM), a technique which enhances the frequency of functional mutants in the libraries, can be used in combination with the screening assays to identify Tango-77 variants (Arkin and Yourvan (1992) *Proc. Natl. Acad. Sci. USA* 89:7811-7815; Delgrave et al. (1993)  
35 *Protein Engineering* 6(3):327-331).

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An isolated Tango-77 protein, or a portion or fragment thereof, can be used as an immunogen to generate antibodies that bind Tango-77 using standard techniques for polyclonal and monoclonal antibody preparation. The  
5 full-length Tango-77 protein can be used or, alternatively, the invention provides antigenic peptide fragments of Tango-77 for use as immunogens. The antigenic peptide of Tango-77 comprises at least 8 (preferably 10, 15, 20, or 30) amino acid residues of the  
10 amino acid sequence shown in SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11 or SEQ ID NO:13 and encompasses an epitope of Tango-77 such that an antibody raised against the peptide forms a specific immune complex with Tango-77.

15 A Tango-77 immunogen typically is used to prepare antibodies by immunizing a suitable subject (e.g., rabbit, goat, mouse or other mammal) with the immunogen. An appropriate immunogenic preparation can contain, for example, recombinantly expressed Tango-77 protein or a  
20 chemically synthesized Tango-77 polypeptide. The preparation can further include an adjuvant, such as Freund's complete or incomplete adjuvant, or similar immunostimulatory agent. Immunization of a suitable subject with an immunogenic Tango-77 preparation induces  
25 a polyclonal anti-Tango-77 antibody response.

Accordingly, another aspect of the invention pertains to anti-Tango-77 antibodies. The term "antibody" as used herein refers to immunoglobulin molecules and immunologically active portions of  
30 immunoglobulin molecules, i.e., molecules that contain an antigen binding site which specifically binds an antigen, such as Tango-77. A molecule which specifically binds to Tango-77 is a molecule which binds Tango-77, but does not substantially bind other molecules in a sample, e.g., a  
35 biological sample, which naturally contains Tango-77.

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Examples of immunologically active portions of immunoglobulin molecules include F(ab) and F(ab')<sub>2</sub> fragments which can be generated by treating the antibody with an enzyme such as pepsin. The invention provides

5 polyclonal and monoclonal antibodies that bind Tango-77. The term "monoclonal antibody" or "monoclonal antibody composition", as used herein, refers to a population of antibody molecules that contain only one species of an antigen binding site capable of immunoreacting with a

10 particular epitope of Tango-77. A monoclonal antibody composition thus typically displays a single binding affinity for a particular Tango-77 protein with which it immunoreacts.

Polyclonal anti-Tango-77 antibodies can be

15 prepared as described above by immunizing a suitable subject with a Tango-77 immunogen. The anti-Tango-77 antibody titer in the immunized subject can be monitored over time by standard techniques, such as with an enzyme linked immunosorbent assay (ELISA) using immobilized

20 Tango-77. If desired, the antibody molecules directed against Tango-77 can be isolated from the mammal (e.g., from the blood) and further purified by well-known techniques, such as protein A chromatography to obtain the IgG fraction. At an appropriate time after

25 immunization, e.g., when the anti-Tango-77 antibody titers are highest, antibody-producing cells can be obtained from the subject and used to prepare monoclonal antibodies by standard techniques, such as the hybridoma technique originally described by Kohler and Milstein

30 (1975) *Nature* 256:495-497, the human B cell hybridoma technique (Kozbor et al. (1983) *Immunol Today* 4:72), the EBV-hybridoma technique (Cole et al. (1985), *Monoclonal Antibodies and Cancer Therapy*, Alan R. Liss, Inc., pp. 77-96) or trioma techniques. The technology for

35 producing hybridomas is well known (see generally Current

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Protocols in Immunology (1994) Coligan et al. (eds.) John Wiley & Sons, Inc., New York, NY). Briefly, an immortal cell line (typically a myeloma) is fused to lymphocytes (typically splenocytes) from a mammal immunized with a  
5 Tango-77 immunogen as described above, and the culture supernatants of the resulting hybridoma cells are screened to identify a hybridoma producing a monoclonal antibody that binds Tango-77.

Any of the many well known protocols used for  
10 fusing lymphocytes and immortalized cell lines can be applied for the purpose of generating an anti-Tango-77 monoclonal antibody (see, e.g., Current Protocols in Immunology, supra; Galfre et al. (1977) Nature 266:55052; R.H. Kenneth, in Monoclonal Antibodies: A New Dimension  
15 In Biological Analyses, Plenum Publishing Corp., New York, New York (1980); and Lerner (1981) Yale J. Biol. Med., 54:387-402. Moreover, the ordinarily skilled worker will appreciate that there are many variations of such methods which also would be useful. Typically, the  
20 immortal cell line (e.g., a myeloma cell line) is derived from the same mammalian species as the lymphocytes. For example, murine hybridomas can be made by fusing lymphocytes from a mouse immunized with an immunogenic preparation of the present invention with an immortalized  
25 mouse cell line, e.g., a myeloma cell line that is sensitive to culture medium containing hypoxanthine, aminopterin and thymidine ("HAT medium"). Any of a number of myeloma cell lines can be used as a fusion partner according to standard techniques, e.g., the P3-  
30 NS1/1-Ag4-1, P3-x63-Ag8.653 or Sp2/O-Ag14 myeloma lines. These myeloma lines are available from ATCC. Typically, HAT-sensitive mouse myeloma cells are fused to mouse splenocytes using polyethylene glycol ("PEG"). Hybridoma cells resulting from the fusion are then selected using  
35 HAT medium, which kills unfused and unproductively fused

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myeloma cells (unfused splenocytes die after several days because they are not transformed). Hybridoma cells producing a monoclonal antibody of the invention are detected by screening the hybridoma culture supernatants  
5 for antibodies that bind Tango-77, e.g., using a standard ELISA assay.

Alternative to preparing monoclonal antibody-secreting hybridomas, a monoclonal anti-Tango-77 antibody can be identified and isolated by screening a recombinant  
10 combinatorial immunoglobulin library (e.g., an antibody phage display library) with Tango-77 to thereby isolate immunoglobulin library members that bind Tango-77. Kits for generating and screening phage display libraries are commercially available (e.g., the Pharmacia Recombinant  
15 Phage Antibody System, Catalog No. 27-9400-01; and the Stratagene SurfZAP™ Phage Display Kit, Catalog No. 240612). Additionally, examples of methods and reagents particularly amenable for use in generating and screening antibody display library can be found in, for example,  
20 U.S. Patent No. 5,223,409; PCT Publication No. WO 92/18619; PCT Publication No. WO 91/17271; PCT Publication No. WO 92/20791; PCT Publication No. WO 92/15679; PCT Publication No. WO 93/01288; PCT Publication No. WO 92/01047; PCT Publication No. WO  
25 92/09690; PCT Publication No. WO 90/02809; Fuchs et al. (1991) *Bio/Technology* 9:1370-1372; Hay et al. (1992) *Hum. Antibod. Hybridomas* 3:81-85; Huse et al. (1989) *Science* 246:1275-1281; Griffiths et al. (1993) *EMBO J* 12:725-734.

Additionally, recombinant anti-Tango-77  
30 antibodies, such as chimeric and humanized monoclonal antibodies, comprising both human and non-human portions, which can be made using standard recombinant DNA techniques, are within the scope of the invention. Such chimeric and humanized monoclonal antibodies can be  
35 produced by recombinant DNA techniques known in the art,

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- for example using methods described in PCT Publication No. WO 87/02671; European Patent Application 184,187; European Patent Application 171,496; European Patent Application 173,494; PCT Publication No. WO 86/01533;
- 5 U.S. Patent No. 4,816,567; European Patent Application 125,023; Better et al. (1988) *Science* 240:1041-1043; Liu et al. (1987) *Proc. Natl. Acad. Sci. USA* 84:3439-3443; Liu et al. (1987) *J. Immunol.* 139:3521-3526; Sun et al. (1987) *Proc. Natl. Acad. Sci. USA* 84:214-218; Nishimura
- 10 et al. (1987) *Canc. Res.* 47:999-1005; Wood et al. (1985) *Nature* 314:446-449; and Shaw et al. (1988) *J. Natl. Cancer Inst.* 80:1553-1559; Morrison (1985) *Science* 229:1202-1207; Oi et al. (1986) *Bio/Techniques* 4:214; U.S. Patent 5,225,539; Jones et al. (1986) *Nature*
- 15 321:552-525; Verhoeyan et al. (1988) *Science* 239:1534; and Beidler et al. (1988) *J. Immunol.* 141:4053-4060.

Completely human antibodies are particularly desirable for therapeutic treatment of human patients. Such antibodies can be produced using transgenic mice

20 which are incapable of expressing endogenous immunoglobulin heavy and light chains genes, but which can express human heavy and light chain genes. The transgenic mice are immunized in the normal fashion with a selected antigen, e.g., all or a portion of Tango-77.

25 Monoclonal antibodies directed against the antigen can be obtained using conventional hybridoma technology. The human immunoglobulin transgenes harbored by the transgenic mice rearrange during B cell differentiation, and subsequently undergo class switching and somatic

30 mutation. Thus, using such a technique, it is possible to produce therapeutically useful IgG, IgA and IgE antibodies. For an overview of this technology for producing human antibodies, see Lonberg and Huszar (1995, *Int. Rev. Immunol.* 13:65-93). For a detailed discussion

35 of this technology for producing human antibodies and

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human monoclonal antibodies and protocols for producing such antibodies, see, e.g., U.S. Patent 5,625,126; U.S. Patent 5,633,425; U.S. Patent 5,569,825; U.S. Patent 5,661,016; and U.S. Patent 5,545,806. In addition, 5 companies such as Abgenix, Inc. (Freemont, CA), can be engaged to provide human antibodies directed against a selected antigen using technology similar to the described above.

Completely human antibodies which recognize a 10 selected epitope can be generated using a technique referred to as "guided selection." In this approach a selected non-human monoclonal antibody, e.g., a murine antibody, is used to guide the selection of a completely human antibody recognizing the same epitope.

15 First, a non-human monoclonal antibody which binds a selected antigen (epitope), e.g., an antibody which inhibits Tango-77 activity, is identified. The heavy chain and the light chain of the non-human antibody are cloned and used to create phage display Fab fragments. 20 For example, the heavy chain gene can be cloned into a plasmid vector so that the heavy chain can be secreted from bacteria. The light chain gene can be cloned into a phage coat protein gene so that the light chain can be expressed on the surface of phage. A repertoire (random 25 collection) of human light chains fused to phage is used to infect the bacteria which express the non-human heavy chain. The resulting progeny phage display hybrid antibodies (human light chain/non-human heavy chain). The selected antigen is used in a panning screen to 30 select phage which bind the selected antigen. Several rounds of selection may be required to identify such phage. Next, human light chain genes are isolated from the selected phage which bind the selected antigen. These selected human light chain genes are then used to 35 guide the selection of human heavy chain genes as

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follows. The selected human light chain genes are inserted into vectors for expression by bacteria. Bacteria expressing the selected human light chains are infected with a repertoire of human heavy chains fused to phage. The resulting progeny phage display human antibodies (human light chain/human heavy chain).

Next, the selected antigen is used in a panning screen to select phage which bind the selected antigen. The phage selected in this step display completely human antibody which recognize the same epitope recognized by the original selected, non-human monoclonal antibody. The genes encoding both the heavy and light chains are readily isolated and be further manipulated for production of human antibody. This technology is described by Jespers et al. (1994, *Bio/technology* 12:899-903).

An anti-Tango-77 antibody (e.g., monoclonal antibody) can be used to isolate Tango-77 by standard techniques, such as affinity chromatography or immunoprecipitation. An anti-Tango-77 antibody can facilitate the purification of natural Tango-77 from cells and of recombinantly produced Tango-77 expressed in host cells. Moreover, an anti-Tango-77 antibody can be used to detect Tango-77 protein (e.g., in a cellular lysate or cell supernatant) in order to evaluate the abundance and pattern of expression of the Tango-77 protein. Anti-Tango-77 antibodies can be used diagnostically to monitor protein levels in tissue as part of a clinical testing procedure, e.g., to, for example, determine the efficacy of a given treatment regimen. Detection can be facilitated by coupling the antibody to a detectable substance. Examples of detectable substances include various enzymes, prosthetic groups, fluorescent materials, luminescent materials, bioluminescent materials, and radioactive materials.



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Examples of suitable enzymes include horseradish peroxidase, alkaline phosphatase,  $\beta$ -galactosidase, or acetylcholinesterase; examples of suitable prosthetic group complexes include streptavidin/biotin and  
5 avidin/biotin; examples of suitable fluorescent materials include umbelliferone, fluorescein, fluorescein isothiocyanate, rhodamine, dichlorotriazinylamine fluorescein, dansyl chloride or phycoerythrin; an example of a luminescent material includes luminol; examples of  
10 bioluminescent materials include luciferase, luciferin, and aequorin, and examples of suitable radioactive material include  $^{125}\text{I}$ ,  $^{131}\text{I}$ ,  $^{35}\text{S}$  or  $^3\text{H}$ .

### III. Recombinant Expression Vectors and Host Cells

Another aspect of the invention pertains to  
15 vectors, preferably expression vectors, containing a nucleic acid molecule encoding Tango-77 (or a portion thereof). As used herein, the term "vector" refers to a nucleic acid molecule capable of transporting another nucleic acid to which it has been linked. One type of  
20 vector is a "plasmid", which refers to a circular double stranded DNA loop into which additional DNA segments can be ligated. Another type of vector is a viral vector, wherein additional DNA segments can be ligated into the viral genome. Certain vectors are capable of autonomous  
25 replication in a host cell into which they are introduced (e.g., bacterial vectors having a bacterial origin of replication and episomal mammalian vectors). Other vectors (e.g., non-episomal mammalian vectors) are integrated into the genome of a host cell upon  
30 introduction into the host cell, and thereby are replicated along with the host genome. Moreover, certain vectors, expression vectors, are capable of directing the expression of genes to which they are operably linked. In general, expression vectors of utility in recombinant

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DNA techniques are often in the form of plasmids (vectors). However, the invention is intended to include such other forms of expression vectors, such as viral vectors (e.g., replication defective retroviruses, adenoviruses and adeno-associated viruses), which serve equivalent functions.

The recombinant expression vectors of the invention comprise a nucleic acid of the invention in a form suitable for expression of the nucleic acid in a host cell, which means that the recombinant expression vectors include one or more regulatory sequences, selected on the basis of the host cells to be used for expression, which is operably linked to the nucleic acid sequence to be expressed. Within a recombinant expression vector, "operably linked" is intended to mean that the nucleotide sequence of interest is linked to the regulatory sequence(s) in a manner which allows for expression of the nucleotide sequence (e.g., in an *in vitro* transcription/translation system or in a host cell when the vector is introduced into the host cell). The term "regulatory sequence" is intended to include promoters, enhancers and other expression control elements (e.g., polyadenylation signals). Such regulatory sequences are described, for example, in Goeddel; *Gene Expression Technology: Methods in Enzymology* 185, Academic Press, San Diego, CA (1990). Regulatory sequences include those which direct constitutive expression of a nucleotide sequence in many types of host cell and those which direct expression of the nucleotide sequence only in certain host cells (e.g., tissue-specific regulatory sequences). It will be appreciated by those skilled in the art that the design of the expression vector can depend on such factors as the choice of the host cell to be transformed, the level of expression of protein desired, etc. The expression

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vectors of the invention can be introduced into host cells to thereby produce proteins or peptides, including fusion proteins or peptides, encoded by nucleic acids as described herein (e.g., Tango-77 proteins, mutant forms of Tango-77, fusion proteins, etc.).

The recombinant expression vectors of the invention can be designed for expression of Tango-77 in prokaryotic or eukaryotic cells, e.g., bacterial cells such as *E. coli*, insect cells (using baculovirus expression vectors), yeast cells or mammalian cells. Suitable host cells are discussed further in Goeddel, *Gene Expression Technology: Methods in Enzymology* 185, Academic Press, San Diego, CA (1990). Alternatively, the recombinant expression vector can be transcribed and translated *in vitro*, for example using T7 promoter regulatory sequences and T7 polymerase.

Expression of proteins in prokaryotes is most often carried out in *E. coli* with vectors containing constitutive or inducible promoters directing the expression of either fusion or non-fusion proteins. Fusion vectors add a number of amino acids to a protein encoded therein, usually to the amino terminus of the recombinant protein. Such fusion vectors typically serve three purposes: 1) to increase expression of recombinant protein; 2) to increase the solubility of the recombinant protein; and 3) to aid in the purification of the recombinant protein by acting as a ligand in affinity purification. Often, in fusion expression vectors, a proteolytic cleavage site is introduced at the junction of the fusion moiety and the recombinant protein to enable separation of the recombinant protein from the fusion moiety subsequent to purification of the fusion protein. Such enzymes, and their cognate recognition sequences, include Factor Xa, thrombin and enterokinase. Typical fusion expression vectors include pGEX (Pharmacia

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Biotech Inc; Smith and Johnson (1988) *Gene* 67:31-40), pMAL (New England Biolabs, Beverly, MA) and pRIT5 (Pharmacia, Piscataway, NJ) which fuse glutathione S-transferase (GST), maltose E binding protein, or protein  
5 A, respectively, to the target recombinant protein.

Examples of suitable inducible non-fusion *E. coli* expression vectors include pTrc (Amann et al. (1988) *Gene* 69:301-315) and pET 11d (Studier et al., *Gene Expression Technology: Methods in Enzymology* 185, Academic Press,  
10 San Diego, California (1990) 60-89). Target gene expression from the pTrc vector relies on host RNA polymerase transcription from a hybrid trp-lac fusion promoter. Target gene expression from the pET 11d vector relies on transcription from a T7 *gn10*-lac fusion  
15 promoter mediated by a coexpressed viral RNA polymerase (T7 *gn1*). This viral polymerase is supplied by host strains BL21(DE3) or HMS174(DE3) from a resident  $\lambda$  prophage harboring a T7 *gn1* gene under the transcriptional control of the *lacUV 5* promoter.

20 One strategy to maximize recombinant protein expression in *E. coli* is to express the protein in a host bacteria with an impaired capacity to proteolytically cleave the recombinant protein (Gottesman, *Gene Expression Technology: Methods in Enzymology* 185,  
25 Academic Press, San Diego, California (1990) 119-128). Another strategy is to alter the nucleic acid sequence of the nucleic acid to be inserted into an expression vector so that the individual codons for each amino acid are those preferentially utilized in *E. coli* (Wada et al.  
30 (1992) *Nucleic Acids Res.* 20:2111-2118). Such alteration of nucleic acid sequences of the invention can be carried out by standard DNA synthesis techniques.

In another embodiment, the Tango-77 expression vector is a yeast expression vector. Examples of vectors  
35 for expression in yeast *S. cerevisiae* include pYepSec1

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(Baldari et al. (1987) *EMBO J.* 6:229-234), pMFa (Kurjan and Herskowitz (1982) *Cell* 30:933-943), pJRY88 (Schultz et al. (1987) *Gene* 54:113-123), pYES2 (Invitrogen Corporation, San Diego, CA), and picZ (Invitrogen Corp, 5 San Diego, CA).

Alternatively, Tango-77 can be expressed in insect cells using baculovirus expression vectors. Baculovirus vectors available for expression of proteins in cultured insect cells (e.g., Sf 9 cells) include the pAc series 10 (Smith et al. (1983) *Mol. Cell Biol.* 3:2156-2165) and the pVL series (Lucklow and Summers (1989) *Virology* 170:31-39).

In yet another embodiment, a nucleic acid of the invention is expressed in mammalian cells using a 15 mammalian expression vector. Examples of mammalian expression vectors include pCDM8 (Seed (1987) *Nature* 329:840) and pMT2PC (Kaufman et al. (1987) *EMBO J.* 6:187-195). When used in mammalian cells, the expression vector's control functions are often provided by viral 20 regulatory elements. For example, commonly used promoters are derived from polyoma, Adenovirus 2, cytomegalovirus and Simian Virus 40. For other suitable expression systems for both prokaryotic and eukaryotic cells see chapters 16 and 17 of Sambrook et al. (*supra*).

25 In another embodiment, the recombinant mammalian expression vector is capable of directing expression of the nucleic acid preferentially in a particular cell type (e.g., tissue-specific regulatory elements are used to express the nucleic acid). Tissue-specific regulatory 30 elements are known in the art. Non-limiting examples of suitable tissue-specific promoters include the albumin promoter (liver-specific; Pinkert et al. (1987) *Genes Dev.* 1:268-277), lymphoid-specific promoters (Calame and Eaton (1988) *Adv. Immunol.* 43:235-275), in particular 35 promoters of T cell receptors (Winoto and Baltimore

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(1989) *EMBO J.* 8:729-733) and immunoglobulins (Banerji et al. (1983) *Cell* 33:729-740; Queen and Baltimore (1983) *Cell* 33:741-748), neuron-specific promoters (e.g., the neurofilament promoter; Byrne and Ruddle (1989) *Proc. Natl. Acad. Sci. USA* 86:5473-5477), pancreas-specific promoters (Edlund et al. (1985) *Science* 230:912-916), and mammary gland-specific promoters (e.g., milk whey promoter; U.S. Patent No. 4,873,316 and European Application Publication No. 264,166). Developmentally-regulated promoters are also encompassed, for example the murine hox promoters (Kessel and Gruss (1990) *Science* 249:374-379) and the  $\alpha$ -fetoprotein promoter (Campes and Tilghman (1989) *Genes Dev.* 3:537-546).

The invention further provides a recombinant expression vector comprising a DNA molecule of the invention cloned into the expression vector in an antisense orientation. That is, the DNA molecule is operably linked to a regulatory sequence in a manner which allows for expression (by transcription of the DNA molecule) of an RNA molecule which is antisense to Tango-77 mRNA. Regulatory sequences operably linked to a nucleic acid cloned in the antisense orientation can be chosen which direct the continuous expression of the antisense RNA molecule in a variety of cell types, for instance viral promoters and/or enhancers, or regulatory sequences can be chosen which direct constitutive, tissue specific or cell type specific expression of antisense RNA. The antisense expression vector can be in the form of a recombinant plasmid, phagemid or attenuated virus in which antisense nucleic acids are produced under the control of a high efficiency regulatory region, the activity of which can be determined by the cell type into which the vector is introduced. For a discussion of the regulation of gene expression using antisense genes see

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Weintraub et al. (*Reviews - Trends in Genetics*, Vol. 1(1) 1986).

Another aspect of the invention pertains to host cells into which a recombinant expression vector of the invention has been introduced. The terms "host cell" and "recombinant host cell" are used interchangeably herein. It is understood that such terms refer not only to the particular subject cell but to the progeny or potential progeny of such a cell. Because certain modifications may occur in succeeding generations due to either mutation or environmental influences, such progeny may not, in fact, be identical to the parent cell, but are still included within the scope of the term as used herein.

A host cell can be any prokaryotic or eukaryotic cell. For example, Tango-77 protein can be expressed in bacterial cells such as *E. coli*, insect cells, yeast or mammalian cells (such as Chinese hamster ovary cells (CHO) or COS cells). Other suitable host cells are known to those skilled in the art.

Vector DNA can be introduced into prokaryotic or eukaryotic cells via conventional transformation or transfection techniques. As used herein, the terms "transformation" and "transfection" are intended to refer to a variety of art-recognized techniques for introducing foreign nucleic acid (e.g., DNA) into a host cell, including calcium phosphate or calcium chloride coprecipitation, DEAE-dextran-mediated transfection, lipofection, or electroporation. Suitable methods for transforming or transfecting host cells can be found in Sambrook, et al. (*supra*), and other laboratory manuals.

For stable transfection of mammalian cells, it is known that, depending upon the expression vector and transfection technique used, only a small fraction of cells may integrate the foreign DNA into their genome.

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In order to identify and select these integrants, a gene that encodes a selectable marker (e.g., for resistance to antibiotics) is generally introduced into the host cells along with the gene of interest. Preferred selectable  
5 markers include those which confer resistance to drugs, such as G418, hygromycin and methotrexate. Nucleic acid encoding a selectable marker can be introduced into a host cell on the same vector as that encoding Tango-77 or can be introduced on a separate vector. Cells stably  
10 transfected with the introduced nucleic acid can be identified by drug selection (e.g., cells that have incorporated the selectable marker gene will survive, while the other cells die).

A host cell of the invention, such as a  
15 prokaryotic or eukaryotic host cell in culture, can be used to produce (i.e., express) Tango-77 protein. Accordingly, the invention further provides methods for producing Tango-77 protein using the host cells of the invention. In one embodiment, the method comprises  
20 culturing the host cell of invention (into which a recombinant expression vector encoding Tango-77 has been introduced) in a suitable medium such that Tango-77 protein is produced. In another embodiment, the method further comprises isolating Tango-77 from the medium or  
25 the host cell.

The host cells of the invention can also be used to produce nonhuman transgenic animals. For example, in one embodiment, a host cell of the invention is a fertilized oocyte or an embryonic stem cell into which  
30 Tango-77-coding sequences have been introduced. Such host cells can then be used to create non-human transgenic animals in which exogenous Tango-77 sequences have been introduced into their genome or homologous recombinant animals in which endogenous Tango-77  
35 sequences have been altered. Such animals are useful for



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studying the function and/or activity of Tango-77 and for identifying and/or evaluating modulators of Tango-77 activity. As used herein, a "transgenic animal" is a non-human animal, preferably a mammal, more preferably a rodent such as a rat or mouse, in which one or more of the cells of the animal includes a transgene. Other examples of transgenic animals include non-human primates, sheep, dogs, cows, goats, chickens, amphibians, etc. A transgene is exogenous DNA which is integrated into the genome of a cell from which a transgenic animal develops and which remains in the genome of the mature animal, thereby directing the expression of an encoded gene product in one or more cell types or tissues of the transgenic animal. As used herein, an "homologous recombinant animal" is a non-human animal, preferably a mammal, more preferably a mouse, in which an endogenous Tango-77 gene has been altered by homologous recombination between the endogenous gene and an exogenous DNA molecule introduced into a cell of the animal, e.g., an embryonic cell of the animal, prior to development of the animal.

A transgenic animal of the invention can be created by introducing Tango-77-encoding nucleic acid into the male pronuclei of a fertilized oocyte, e.g., by microinjection, retroviral infection, and allowing the oocyte to develop in a pseudopregnant female foster animal. The Tango-77 cDNA sequence e.g., that of (SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6; SEQ ID NO:10 or the cDNA of ATCC 98807) can be introduced as a transgene into the genome of a non-human animal. Alternatively, a nonhuman homologue of the human Tango-77 gene, such as a mouse Tango-77 gene, can be isolated based on hybridization to the human Tango-77 cDNA and used as a transgene. Intronic sequences and polyadenylation signals can also be included in the transgene to increase the efficiency

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of expression of the transgene. A tissue-specific regulatory sequence(s) can be operably linked to the Tango-77 transgene to direct expression of Tango-77 protein to particular cells. Methods for generating transgenic animals via embryo manipulation and microinjection, particularly animals such as mice, have become conventional in the art and are described, for example, in U.S. Patent Nos. 4,736,866 and 4,870,009, U.S. Patent No. 4,873,191 and in Hogan, *Manipulating the Mouse Embryo* (Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., 1986). Similar methods are used for production of other transgenic animals. A transgenic founder animal can be identified based upon the presence of the Tango-77 transgene in its genome and/or expression of Tango-77 mRNA in tissues or cells of the animals. A transgenic founder animal can then be used to breed additional animals carrying the transgene. Moreover, transgenic animals carrying a transgene encoding Tango-77 can further be bred to other transgenic animals carrying other transgenes.

To create an homologous recombinant animal, a vector is prepared which contains at least a portion of a Tango-77 gene (e.g., a human or a non-human homolog of the Tango-77 gene, e.g., a murine Tango-77 gene) into which a deletion, addition or substitution has been introduced to thereby alter, e.g., functionally disrupt, the Tango-77 gene. In a preferred embodiment, the vector is designed such that, upon homologous recombination, the endogenous Tango-77 gene is functionally disrupted (i.e., no longer encodes a functional protein; also referred to as a "knock out" vector). Alternatively, the vector can be designed such that, upon homologous recombination, the endogenous Tango-77 gene is mutated or otherwise altered but still encodes functional protein (e.g., the upstream regulatory region can be altered to thereby

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alter the expression of the endogenous Tango-77 protein). In the homologous recombination vector, the altered portion of the Tango-77 gene is flanked at its 5' and 3' ends by additional nucleic acid of the Tango-77 gene to  
5 allow for homologous recombination to occur between the exogenous Tango-77 gene carried by the vector and an endogenous Tango-77 gene in an embryonic stem cell. The additional flanking Tango-77 nucleic acid is of sufficient length for successful homologous recombination  
10 with the endogenous gene. Typically, several kilobases of flanking DNA (both at the 5' and 3' ends) are included in the vector (see, e.g., Thomas and Capecchi (1987) *Cell* 51:503 for a description of homologous recombination vectors). The vector is introduced into an embryonic  
15 stem cell line (e.g., by electroporation) and cells in which the introduced Tango-77 gene has homologously recombined with the endogenous Tango-77 gene are selected (see, e.g., Li et al. (1992) *Cell* 69:915). The selected cells are then injected into a blastocyst of an animal  
20 (e.g., a mouse) to form aggregation chimeras (see, e.g., Bradley in *Teratocarcinomas and Embryonic Stem Cells: A Practical Approach*, Robertson, ed. (IRL, Oxford, 1987) pp. 113-152). A chimeric embryo can then be implanted into a suitable pseudopregnant female foster animal and  
25 the embryo brought to term. Progeny harboring the homologously recombined DNA in their germ cells can be used to breed animals in which all cells of the animal contain the homologously recombined DNA by germline transmission of the transgene. Methods for constructing  
30 homologous recombination vectors and homologous recombinant animals are described further in Bradley (1991) *Current Opinion in Bio/Technology* 2:823-829 and in PCT Publication Nos. WO 90/11354, WO 91/01140, WO 92/0968, and WO 93/04169.

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In another embodiment, transgenic non-human animals can be produced which contain selected systems which allow for regulated expression of the transgene. One example of such a system is the cre/loxP recombinase system of bacteriophage P1. For a description of the cre/loxP recombinase system, see, e.g., Lakso et al. (1992) *Proc. Natl. Acad. Sci. USA* 89:6232-6236. Another example of a recombinase system is the FLP recombinase system of *Saccharomyces cerevisiae* (O'Gorman et al. (1991) *Science* 251:1351-1355. If a cre/loxP recombinase system is used to regulate expression of the transgene, animals containing transgenes encoding both the Cre recombinase and a selected protein are required. Such animals can be provided through the construction of "double" transgenic animals, e.g., by mating two transgenic animals, one containing a transgene encoding a selected protein and the other containing a transgene encoding a recombinase.

Clones of the non-human transgenic animals described herein can also be produced according to the methods described in Wilmut et al. (1997) *Nature* 385:810-813 and PCT Publication Nos. WO 97/07668 and WO 97/07669. In brief, a cell, e.g., a somatic cell, from the transgenic animal can be isolated and induced to exit the growth cycle and enter G<sub>0</sub> phase. The quiescent cell can then be fused, e.g., through the use of electrical pulses, to an enucleated oocyte from an animal of the same species from which the quiescent cell is isolated. The reconstructed oocyte is then cultured such that it develops to morula or blastocyte and then transferred to pseudopregnant female foster animal. The offspring borne of this female foster animal will be a clone of the animal from which the cell, e.g., the somatic cell, is isolated.

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#### IV. Pharmaceutical Compositions

The Tango-77 nucleic acid molecules, Tango-77 proteins, and anti-Tango-77 antibodies (also referred to herein as "active compounds") of the invention can be  
5 incorporated into pharmaceutical compositions suitable for administration. Such compositions typically comprise the nucleic acid molecule, protein, or antibody and a pharmaceutically acceptable carrier. As used herein the language "pharmaceutically acceptable carrier" is  
10 intended to include any and all solvents, dispersion media, coatings, antibacterial and antifungal agents, isotonic and absorption delaying agents, and the like, compatible with pharmaceutical administration. The use of such media and agents for pharmaceutically active  
15 substances is well known in the art. Except insofar as any conventional media or agent is incompatible with the active compound, use thereof in the compositions is contemplated. Supplementary active compounds can also be incorporated into the compositions.

20 A pharmaceutical composition of the invention is formulated to be compatible with its intended route of administration. Examples of routes of administration include parenteral, (e.g. intravenous, intradermal, subcutaneous) (e.g., oral inhalation), transdermal  
25 (topical), transmucosal, and rectal administration. Solutions or suspensions used for parenteral, intradermal, or subcutaneous application can include the following components: a sterile diluent such as water for injection, saline solution, fixed oils, polyethylene  
30 glycols, glycerine, propylene glycol or other synthetic solvents; antibacterial agents such as benzyl alcohol or methyl parabens; antioxidants such as ascorbic acid or sodium bisulfite; chelating agents such as ethylenediaminetetraacetic acid; buffers such as  
35 acetates, citrates or phosphates and agents for the

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adjustment of tonicity such as sodium chloride or dextrose. pH can be adjusted with acids or bases, such as hydrochloric acid or sodium hydroxide. The parenteral preparation can be enclosed in ampoules, disposable  
5 syringes or multiple dose vials made of glass or plastic.

Pharmaceutical compositions suitable for injectable use include sterile aqueous solutions (where water soluble) or dispersions and sterile powders for the extemporaneous preparation of sterile injectable  
10 solutions or dispersions. For intravenous administration, suitable carriers include physiological saline, bacteriostatic water, Cremophor EL™ (BASF; Parsippany, NJ) or phosphate buffered saline (PBS). In all cases, the composition must be sterile and should be  
15 fluid to the extent that easy syringability exists. It must be stable under the conditions of manufacture and storage and must be preserved against the contaminating action of microorganisms such as bacteria and fungi. The carrier can be a solvent or dispersion medium containing,  
20 for example, water, ethanol, polyol (for example, glycerol, propylene glycol, and liquid polyethylene glycol, and the like), and suitable mixtures thereof. The proper fluidity can be maintained, for example, by the use of a coating such as lecithin, by the maintenance  
25 of the required particle size in the case of dispersion and by the use of surfactants. Prevention of the action of microorganisms can be achieved by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, ascorbic acid,  
30 thimerosal, and the like. In many cases, it will be preferable to include isotonic agents, for example, sugars, polyalcohols such as mannitol, sorbitol, sodium chloride in the composition. Prolonged absorption of the injectable compositions can be brought about by including

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in the composition an agent which delays absorption, for example, aluminum monostearate and gelatin.

Sterile injectable solutions can be prepared by incorporating the active compound (e.g., a Tango-77 protein or anti-Tango-77 antibody) in the required amount in an appropriate solvent with one or a combination of ingredients enumerated above, as required, followed by filtered sterilization. Generally, dispersions are prepared by incorporating the active compound into a sterile vehicle which contains a basic dispersion medium and the required other ingredients from those enumerated above. In the case of sterile powders for the preparation of sterile injectable solutions, the preferred methods of preparation are vacuum drying and freeze-drying which yields a powder of the active ingredient plus any additional desired ingredient from a previously sterile-filtered solution thereof.

Oral compositions generally include an inert diluent or an edible carrier. They can be enclosed in gelatin capsules or compressed into tablets. For the purpose of oral therapeutic administration, the active compound can be incorporated with excipients and used in the form of tablets, troches, or capsules. Oral compositions can also be prepared using a fluid carrier for use as a mouthwash, wherein the compound in the fluid carrier is applied orally and swished and expectorated or swallowed. Pharmaceutically compatible binding agents, and/or adjuvant materials can be included as part of the composition. The tablets, pills, capsules, troches and the like can contain any of the following ingredients, or compounds of a similar nature: a binder such as microcrystalline cellulose, gum tragacanth or gelatin; an excipient such as starch or lactose, a disintegrating agent such as alginic acid, Primogel, or corn starch; a lubricant such as magnesium stearate or Sterotes; a

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glidant such as colloidal silicon dioxide; a sweetening agent such as sucrose or saccharin; or a flavoring agent such as peppermint, methyl salicylate, or orange flavoring.

5 For administration by inhalation, the compounds are delivered in the form of an aerosol spray from a pressurized container or dispenser which contains a suitable propellant, e.g., a gas such as carbon dioxide, or a nebulizer.

10 Systemic administration can also be by transmucosal or transdermal means. For transmucosal or transdermal administration, penetrants appropriate to the barrier to be permeated are used in the formulation. Such penetrants are generally known in the art, and  
15 include, for example, for transmucosal administration, detergents, bile salts, and fusidic acid derivatives. Transmucosal administration can be accomplished through the use of nasal sprays or suppositories. For  
20 transdermal administration, the active compounds are formulated into ointments, salves, gels, or creams as generally known in the art.

The compounds can also be prepared in the form of suppositories (e.g., with conventional suppository bases such as cocoa butter and other glycerides) or retention  
25 enemas for rectal delivery.

In one embodiment, the active compounds are prepared with carriers that will protect the compound against rapid elimination from the body, such as a controlled release formulation, including implants and  
30 microencapsulated delivery systems. Biodegradable, biocompatible polymers can be used, such as ethylene vinyl acetate, polyanhydrides, polyglycolic acid, collagen, polyorthoesters, and polylactic acid. Methods for preparation of such formulations will be apparent to  
35 those skilled in the art. The materials can also be



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obtained commercially from Alza Corporation and Nova Pharmaceuticals, Inc. Liposomal suspensions (including liposomes targeted to infected cells with monoclonal antibodies to viral antigens) can also be used as  
5 pharmaceutically acceptable carriers. These can be prepared according to methods known to those skilled in the art, for example, as described in U.S. Patent No. 4,522,811.

It is especially advantageous to formulate oral or  
10 parenteral compositions in dosage unit form for ease of administration and uniformity of dosage. Dosage unit form as used herein refers to physically discrete units suited as unitary dosages for the subject to be treated; each unit containing a predetermined quantity of active  
15 compound calculated to produce the desired therapeutic effect in association with the required pharmaceutical carrier. The specification for the dosage unit forms of the invention are dictated by and directly dependent on the unique characteristics of the active compound and the  
20 particular therapeutic effect to be achieved, and the limitations inherent in the art of compounding such an active compound for the treatment of individuals.

The nucleic acid molecules of the invention can be inserted into vectors and used as gene therapy vectors.  
25 Gene therapy vectors can be delivered to a subject by, for example, intravenous injection, local administration (U.S. Patent 5,328,470) or by stereotactic injection (see, e.g., Chen et al. (1994) *Proc. Natl. Acad. Sci. USA* 91:3054-3057). The pharmaceutical preparation of the  
30 gene therapy vector can include the gene therapy vector in an acceptable diluent, or can comprise a slow release matrix in which the gene delivery vehicle is imbedded. Alternatively, where the complete gene delivery vector can be produced intact from recombinant cells, e.g.  
35 retroviral vectors, the pharmaceutical preparation can

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include one or more cells which produce the gene delivery system.

The pharmaceutical compositions can be included in a container, pack, or dispenser together with  
5 instructions for administration.

#### V. Uses and Methods of the Invention

The nucleic acid molecules, proteins, protein homologues, and antibodies described herein can be used in one or more of the following methods: a) screening  
10 assays; b) detection assays (e.g., chromosomal mapping, tissue typing, forensic biology); c) predictive medicine (e.g., diagnostic assays, prognostic assays, monitoring clinical trials, and pharmacogenomics); and d) methods of treatment (e.g., therapeutic and prophylactic). A  
15 Tango-77 protein interacts with other cellular proteins and can thus be used for regulation of inflammation. The polypeptides of the invention can be used in assays to determine biological activity. For example, they could be used in a panel of proteins for high-throughput  
20 screening.

The isolated nucleic acid molecules of the invention can be used to express Tango-77 protein (e.g., via a recombinant expression vector in a host cell in gene therapy applications), to detect Tango-77 mRNA  
25 (e.g., in a biological sample) or a genetic lesion in a Tango-77 gene, and to modulate Tango-77 activity. In addition, the Tango-77 proteins can be used to screen drugs or compounds which modulate the Tango-77 activity or expression as well as to treat disorders characterized  
30 by insufficient or excessive production of Tango-77 protein or production of Tango-77 protein forms which have decreased or aberrant activity compared to Tango-77 wild type protein. In addition, the anti-Tango-77

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antibodies of the invention can be used to detect and isolate Tango-77 proteins and modulate Tango-77 activity.

This invention further pertains to novel agents identified by the above-described screening assays and  
5 uses thereof for treatments as described herein.

#### A. Screening Assays

The invention provides a method (also referred to herein as a "screening assay") for identifying modulators, i.e., candidate or test compounds or agents  
10 (e.g., peptides, peptidomimetics, small molecules or other drugs) which bind to Tango-77 proteins or have a stimulatory or inhibitory effect on, for example, Tango-77 expression or Tango-77 activity.

Examples of methods for the synthesis of molecular  
15 libraries can be found in the art, for example in:  
DeWitt et al. (1993) *Proc. Natl. Acad. Sci. USA* 90:6909;  
Erb et al. (1994) *Proc. Natl. Acad. Sci. USA* 91:11422;  
Zuckermann et al. (1994). *J. Med. Chem.* 37:2678; Cho et al. (1993) *Science* 261:1303; Carrell et al. (1994) *Angew. Chem. Int. Ed. Engl.* 33:2059; Carell et al. (1994) *Angew. Chem. Int. Ed. Engl.* 33:2061; and Gallop et al. (1994) *J. Med. Chem.* 37:1233.

Libraries of compounds may be presented in solution (e.g., Houghten (1992) *Bio/Techniques* 13:412-  
25 421), or on beads (Lam (1991) *Nature* 354:82-84), chips (Fodor (1993) *Nature* 364:555-556), bacteria (U.S. Patent No. 5,223,409), spores (Patent Nos. 5,571,698; 5,403,484; and 5,223,409), plasmids (Cull et al. (1992) *Proc. Natl. Acad. Sci. USA* 89:1865-1869) or phage (Scott and Smith  
30 (1990) *Science* 249:386-390; Devlin (1990) *Science* 249:404-406; Cwirla et al. (1990) *Proc. Natl. Acad. Sci. USA* 87:6378-6382; and Felici (1991) *J. Mol. Biol.* 222:301-310).

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In another embodiment, an assay is used to determine the ability of the test compound to modulate the activity of Tango-77 or a biologically active portion thereof, for example, by determining the ability of the

5 Tango-77 protein to bind to or interact with a Tango-77 target molecule. As used herein, a "target molecule" is a molecule with which a Tango-77 protein binds or interacts in nature, for example, a molecule on the surface of a cell. A Tango-77 target molecule can be a

10 non-Tango-77 molecule or a Tango-77 protein or polypeptide of the present invention. In one embodiment, a Tango-77 target molecule is a component of a signal transduction pathway, for example, Tango-77 may bind to a IL-1 receptor or another receptor thereby blocking the

15 receptor and inhibiting future signal transduction. Determining the ability of the Tango-77 protein to bind to or interact with a Tango-77 target molecule can be accomplished by one of the methods described above. In a preferred embodiment, determining the ability of the

20 Tango-77 protein to bind to or interact with a Tango-77 target molecule can be accomplished by determining the activity of the target molecule. For example, the activity of the target molecule can be determined by detecting induction of a cellular second messenger of the

25 target (e.g., intracellular  $\text{Ca}^{2+}$ , diacylglycerol, IP3, etc.), detecting catalytic/enzymatic activity of the target on an appropriate substrate, detecting the induction of a reporter gene (e.g., a Tango-77-responsive regulatory element operably linked to a nucleic acid

30 encoding a detectable marker, e.g. luciferase), or detecting a cellular response, for example, inflammation.

In yet another embodiment, an assay of the present invention is a cell-free assay comprising contacting a Tango-77 protein or biologically active portion thereof

35 with a test compound and determining the ability of the

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test compound to bind to the Tango-77 protein or biologically active portion thereof. Binding of the test compound to the Tango-77 protein can be determined either directly or indirectly as described above. In a preferred embodiment, the assay includes contacting the Tango-77 protein or biologically active portion thereof with a known compound which binds Tango-77 to form an assay mixture, contacting the assay mixture with a test compound, and determining the ability of the test compound to interact with a Tango-77 protein, wherein determining the ability of the test compound to interact with a Tango-77 protein comprises determining the ability of the test compound to preferentially bind to Tango-77 or biologically active portion thereof as compared to the known compound.

In another embodiment, an assay is a cell-free assay comprising contacting Tango-77 protein or biologically active portion thereof with a test compound and determining the ability of the test compound to modulate (e.g., stimulate or inhibit) the activity of the Tango-77 protein or biologically active portion thereof. Determining the ability of the test compound to modulate the activity of Tango-77 can be accomplished, for example, by determining the ability of the Tango-77 protein to bind to a Tango-77 target molecule by one of the methods described above for determining direct binding. In an alternative embodiment, determining the ability of the test compound to modulate the activity of Tango-77 can be accomplished by determining the ability of the Tango-77 protein to further modulate a Tango-77 target molecule. For example, the catalytic/enzymatic activity of the target molecule on an appropriate substrate can be determined as previously described.

In yet another embodiment, the cell-free assay comprises contacting the Tango-77 protein or biologically

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active portion thereof with a known compound which binds Tango-77 to form an assay mixture, contacting the assay mixture with a test compound, and determining the ability of the test compound to interact with a Tango-77 protein, wherein determining the ability of the test compound to interact with a Tango-77 protein comprises determining the ability of the Tango-77 protein to preferentially bind to or modulate the activity of a Tango-77 target molecule.

10 It is possible that membrane-bound forms of Tango-77 exist. The cell-free assays of the present invention are amenable to use of both the forms Tango-77. In the case of cell-free assays comprising a membrane-bound form of Tango-77, it may be desirable to utilize a  
15 solubilizing agent such that the membrane-bound form of Tango-77 is maintained in solution. Examples of such solubilizing agents include non-ionic detergents such as n-octylglucoside, n-dodecylglucoside, n-dodecylmaltoside, octanoyl-N-methylglucamide, decanoyl-N-methylglucamide,  
20 Triton® X-100, Triton® X-114, Thesit®, Isotridecypoly(ethylene glycol ether)n, 3-[(3-cholamidopropyl)dimethylamminio]-1-propane sulfonate (CHAPS), 3-[(3-cholamidopropyl)dimethylamminio]-2-hydroxy-1-propane sulfonate (CHAPSO), or N-dodecyl=N,N-  
25 dimethyl-3-ammonio-1-propane sulfonate.

In more than one embodiment of the above assay methods of the present invention, it may be desirable to immobilize either Tango-77 or its target molecule to facilitate separation of complexed from uncomplexed forms  
30 of one or both of the proteins, as well as to accommodate automation of the assay. Binding of a test compound to Tango-77, or interaction of Tango-77 with a target molecule in the presence and absence of a candidate compound, can be accomplished in any vessel suitable for  
35 containing the reactants. Examples of such vessels

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include microtitre plates, test tubes, and micro-centrifuge tubes. In one embodiment, a fusion protein can be provided which adds a domain that allows one or both of the proteins to be bound to a matrix. For  
5 example, glutathione-S-transferase/ Tango-77 fusion proteins or glutathione-S-transferase/target fusion proteins can be adsorbed onto glutathione sepharose beads (Sigma Chemical Co.; St. Louis, MO) or glutathione derivatized microtitre plates, which are then combined  
10 with the test compound or the test compound and either the non-adsorbed target protein or Tango-77 protein, and the mixture incubated under conditions conducive to complex formation (e.g., at physiological conditions for salt and pH). Following incubation, the beads or  
15 microtitre plate wells are washed to remove any unbound components and complex formation is measured either directly or indirectly, for example, as described above. Alternatively, the complexes can be dissociated from the matrix, and the level of Tango-77 binding or activity  
20 determined using standard techniques.

Other techniques for immobilizing proteins on matrices can also be used in the screening assays of the invention. For example, either Tango-77 or its target molecule can be immobilized utilizing conjugation of  
25 biotin and streptavidin. Biotinylated Tango-77 or target molecules can be prepared from biotin-NHS (N-hydroxy-succinimide) using techniques well known in the art (e.g., biotinylation kit, Pierce Chemicals; Rockford, IL), and immobilized in the wells of streptavidin-coated  
30 96 well plates (Pierce Chemical). Alternatively, antibodies reactive with Tango-77 or target molecules but which do not interfere with binding of the Tango-77 protein to its target molecule can be derivatized to the wells of the plate, and unbound target or Tango-77  
35 trapped in the wells by antibody conjugation. Methods

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for detecting such complexes, in addition to those described above for the GST-immobilized complexes, include immunodetection of complexes using antibodies reactive with the Tango-77 or target molecule, as well as  
5 enzyme-linked assays which rely on detecting an enzymatic activity associated with the Tango-77 or target molecule.

In another embodiment, modulators of Tango-77 expression are identified in a method in which a cell is contacted with a candidate compound and the expression of  
10 Tango-77 mRNA or protein in the cell is determined. The level of expression of Tango-77 mRNA or protein in the presence of the candidate compound is compared to the level of expression of Tango-77 mRNA or protein in the absence of the candidate compound. The candidate  
15 compound can then be identified as a modulator of Tango-77 expression based on this comparison. For example, when expression of Tango-77 mRNA or protein is greater (statistically significantly greater) in the presence of the candidate compound than in its absence,  
20 the candidate compound is identified as a stimulator of Tango-77 mRNA or protein expression. Alternatively, when expression of Tango-77 mRNA or protein is less (statistically significantly less) in the presence of the candidate compound than in its absence, the candidate  
25 compound is identified as an inhibitor of Tango-77 mRNA or protein expression. The level of Tango-77 mRNA or protein expression in the cells can be determined by methods described herein for detecting Tango-77 mRNA or protein.

30 In yet another aspect of the invention, the Tango-77 proteins can be used as "bait proteins" in a two-hybrid assay or three hybrid assay (see, e.g., U.S. Patent No. 5,283,317; Zervos et al. (1993) *Cell* 72:223-232; Madura et al. (1993) *J. Biol. Chem.* 268:12046-12054;  
35 Bartel et al. (1993) *Bio/Techniques* 14:920-924; Iwabuchi



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et al. (1993) *Oncogene* 8:1693-1696; and PCT Publication No. WO 94/10300), to identify other proteins, which bind to or interact with Tango-77 ("Tango-77-binding proteins" or "Tango-77-bp") and modulate Tango-77 activity. Such  
5 Tango-77-binding proteins are also likely to be involved in the propagation of signals by the Tango-77 proteins as, for example, upstream or downstream elements of the Tango-77 pathway.

The two-hybrid system is based on the modular  
10 nature of most transcription factors, which consist of separable DNA-binding and activation domains. Briefly, the assay utilizes two different DNA constructs. In one construct, the gene that codes for Tango-77 is fused to a gene encoding the DNA binding domain of a known  
15 transcription factor (e.g., GAL-4). In the other construct, a DNA sequence, from a library of DNA sequences, that encodes an unidentified protein ("prey" or "sample") is fused to a gene that codes for the activation domain of the known transcription factor. If  
20 the "bait" and the "prey" proteins are able to interact, *in vivo*, forming an Tango-77-dependent complex, the DNA-binding and activation domains of the transcription factor are brought into close proximity. This proximity allows transcription of a reporter gene (e.g., LacZ)  
25 which is operably linked to a transcriptional regulatory site responsive to the transcription factor. Expression of the reporter gene can be detected and cell colonies containing the functional transcription factor can be isolated and used to obtain the cloned gene which encodes  
30 the protein which interacts with Tango-77.

This invention further pertains to novel agents identified by the above-described screening assays and uses thereof for treatments as described herein.

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## B. Detection Assays

Portions or fragments of the cDNA sequence identified herein (and the corresponding complete gene sequences) can be used in numerous ways as polynucleotide reagents. For example, the sequence can be used to: (i) map the respective gene on a chromosome and, thus, locate gene regions associated with genetic disease; (ii) identify an individual from a minute biological sample (tissue typing); and (iii) aid in forensic identification of a biological sample. These applications are described in the subsections below.

### 1. Chromosome Mapping

Once the sequence (or a portion of the sequence) of a gene has been isolated, this sequence can be used to map the location of the gene on a chromosome. Accordingly, Tango-77 nucleic acid molecules described herein or fragments thereof, can be used to map the location of the Tango-77 gene(s) on a chromosome. The mapping of the Tango-77 sequences to chromosomes is an important first step in correlating these sequences with genes associated with disease.

Briefly, a Tango-77 gene can be mapped to chromosomes by preparing PCR primers (preferably 15-25 bp in length) from the Tango-77 sequences. Computer analysis of Tango-77 sequences can be used to rapidly select primers that do not span more than one exon in the genomic DNA, thus complicating the amplification process. These primers can then be used for PCR screening of somatic cell hybrids containing individual human chromosomes. Only those hybrids containing the human gene corresponding to the Tango-77 sequences will yield an amplified fragment.

Somatic cell hybrids are prepared by fusing somatic cells from different mammals (e.g., human and

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mouse cells). As hybrids of human and mouse cells grow and divide, they gradually lose human chromosomes in random order, but retain the mouse chromosomes. By using media in which mouse cells cannot grow (because they lack a particular enzyme) but in which human cells can, the one human chromosome that contains the gene encoding the needed enzyme, will be retained. By using various media, panels of hybrid cell lines can be established. Each cell line in a panel contains either a single human chromosome or a small number of human chromosomes, and a full set of mouse chromosomes, allowing easy mapping of individual genes to specific human chromosomes. (D'Eustachio et al. (1983) *Science* 220:919-924). Somatic cell hybrids containing only fragments of human chromosomes can also be produced by using human chromosomes with translocations and deletions.

PCR mapping of somatic cell hybrids is a rapid procedure for assigning a particular sequence to a particular chromosome. Three or more sequences can be assigned per day using a single thermal cycler. Using the Tango-77 sequences to design oligonucleotide primers, sublocalization can be achieved with panels of fragments from specific chromosomes. Other mapping strategies which can similarly be used to map a Tango-77 sequence to its chromosome include *in situ* hybridization (described in Fan et al. (1990) *Proc. Natl. Acad. Sci. USA* 87:6223-27), pre-screening with labeled flow-sorted chromosomes, and pre-selection by hybridization to chromosome specific cDNA libraries.

Fluorescence *in situ* hybridization (FISH) of a DNA sequence to a metaphase chromosomal spread can further be used to provide a precise chromosomal location in one step. Chromosome spreads can be made using cells whose division has been blocked in metaphase by a chemical, e.g., colcemid that disrupts the mitotic spindle. The

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chromosomes can be treated briefly with trypsin, and then stained with Giemsa. A pattern of light and dark bands develops on each chromosome, so that the chromosomes can be identified individually. The FISH technique can be  
5 used with a DNA sequence as short as 500 or 600 bases. However, clones larger than 1,000 bases have a higher likelihood of binding to a unique chromosomal location with sufficient signal intensity for simple detection. Preferably 1,000 bases, and more preferably 2,000 bases  
10 will suffice to get good results at a reasonable amount of time. For a review of this technique, see Verma et al. (Human Chromosomes: A Manual of Basic Techniques (Pergamon Press, New York, 1988)).

Reagents for chromosome mapping can be used  
15 individually to mark a single chromosome or a single site on that chromosome, or panels of reagents can be used for marking multiple sites and/or multiple chromosomes. Reagents corresponding to noncoding regions of the genes actually are preferred for mapping purposes. Coding  
20 sequences are more likely to be conserved within gene families, thus increasing the chance of cross hybridizations during chromosomal mapping.

Once a sequence has been mapped to a precise chromosomal location, the physical position of the  
25 sequence on the chromosome can be correlated with genetic map data. (Such data are found, for example, in V. McKusick, Mendelian Inheritance in Man, available on-line through Johns Hopkins University Welch Medical Library). The relationship between genes and disease, mapped to the  
30 same chromosomal region, can then be identified through linkage analysis (co-inheritance of physically adjacent genes), described in, e.g., Egeland et al. (1987) Nature 325:783-787.

Moreover, differences in the DNA sequences between  
35 individuals affected and unaffected with a disease

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associated with the Tango-77 gene can be determined. If a mutation is observed in some or all of the affected individuals but not in any unaffected individuals, then the mutation is likely to be the causative agent of the particular disease. Comparison of affected and unaffected individuals generally involves first looking for structural alterations in the chromosomes such as deletions or translocations that are visible from chromosome spreads or detectable using PCR based on that DNA sequence. Ultimately, complete sequencing of genes from several individuals can be performed to confirm the presence of a mutation and to distinguish mutations from polymorphisms.

## 2. Tissue Typing

The Tango-77 sequences of the present invention can also be used to identify individuals from minute biological samples. The United States military, for example, is considering the use of restriction fragment length polymorphism (RFLP) for identification of its personnel. In this technique, an individual's genomic DNA is digested with one or more restriction enzymes, and probed on a Southern blot to yield unique bands for identification. This method does not suffer from the current limitations of "Dog Tags" which can be lost, switched, or stolen, making positive identification difficult. The sequences of the present invention are useful as additional DNA markers for RFLP (described in U.S. Patent 5,272,057).

Furthermore, the sequences of the present invention can be used to provide an alternative technique which determines the actual base-by-base DNA sequence of selected portions of an individual's genome. Thus, the Tango-77 sequences described herein can be used to prepare two PCR primers from the 5' and 3' ends of the

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sequences. These primers can then be used to amplify an individual's DNA and subsequently sequence it.

Panels of corresponding DNA sequences from individuals, prepared in this manner, can provide unique individual identifications, as each individual will have a unique set of such DNA sequences due to allelic differences. The sequences of the present invention can be used to obtain such identification sequences from individuals and from tissue. The Tango-77 sequences of the invention uniquely represent portions of the human genome. Allelic variation occurs to some degree in the coding regions of these sequences, and to a greater degree in the noncoding regions. It is estimated that allelic variation between individual humans occurs with a frequency of about once per each 500 bases. Each of the sequences described herein can, to some degree, be used as a standard against which DNA from an individual can be compared for identification purposes. Because greater numbers of polymorphisms occur in the noncoding regions, fewer sequences are necessary to differentiate individuals. The noncoding sequences of SEQ ID NO:1 can comfortably provide positive individual identification with a panel of perhaps 10 to 1,000 primers which each yield a noncoding amplified sequence of 100 bases. If predicted coding sequences, such as those in SEQ ID NO:3, SEQ ID NO:6, or SEQ ID NO:10 are used, a more appropriate number of primers for positive individual identification would be 500-2,000.

If a panel of reagents from Tango-77 sequences described herein is used to generate a unique identification database for an individual, those same reagents can later be used to identify tissue from that individual. Using the unique identification database, positive identification of the individual, living or dead, can be made from extremely small tissue samples.

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### 3. Use of Partial Tango-77 Sequences in Forensic Biology

DNA-based identification techniques can also be used in forensic biology. Forensic biology is a scientific field employing genetic typing of biological evidence found at a crime scene as a means for positively identifying, for example, a perpetrator of a crime. To make such an identification, PCR technology can be used to amplify DNA sequences taken from very small biological samples such as tissues, e.g., hair or skin, or body fluids, e.g., blood, saliva, or semen found at a crime scene. The amplified sequence can then be compared to a standard, thereby allowing identification of the origin of the biological sample.

The sequences of the present invention can be used to provide polynucleotide reagents, e.g., PCR primers, targeted to specific loci in the human genome, which can enhance the reliability of DNA-based forensic identifications by, for example, providing another "identification marker" (i.e. another DNA sequence that is unique to a particular individual). As mentioned above, actual base sequence information can be used for identification as an accurate alternative to patterns formed by restriction enzyme generated fragments. Sequences targeted to noncoding regions of SEQ ID NO:1 are particularly appropriate for this use as greater numbers of polymorphisms occur in the noncoding regions, making it easier to differentiate individuals using this technique. Examples of polynucleotide reagents include the Tango-77 sequences or portions thereof, e.g., fragments derived from the noncoding regions of SEQ ID NO:1 having a length of at least 20 or 30 bases.

The Tango-77 sequences described herein can further be used to provide polynucleotide reagents, e.g., labeled or labelable probes which can be used in, for

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example, an in situ hybridization technique, to identify a specific tissue, e.g., brain tissue. This can be very useful in cases where a forensic pathologist is presented with a tissue of unknown origin. Panels of such Tango-77 probes can be used to identify tissue by species and/or by organ type.

In a similar fashion, these reagents, e.g., Tango-77 primers or probes can be used to screen tissue culture for contamination (i.e., screen for the presence of a mixture of different types of cells in a culture).

### C. Predictive Medicine

The present invention also pertains to the field of predictive medicine in which diagnostic assays, prognostic assays, pharmacogenomics, and monitoring clinical trails are used for prognostic (predictive) purposes to thereby treat an individual prophylactically. Accordingly, one aspect of the present invention relates to diagnostic assays for determining Tango-77 protein and/or nucleic acid expression as well as Tango-77 activity, in the context of a biological sample (e.g., blood, serum, cells, tissue) to thereby determine whether an individual is afflicted with a disease or disorder, or is at risk of developing a disorder, associated with aberrant Tango-77 expression or activity. The invention also provides for prognostic (or predictive) assays for determining whether an individual is at risk of developing a disorder associated with Tango-77 protein, nucleic acid expression or activity. For example, mutations in a Tango-77 gene can be assayed in a biological sample. Such assays can be used for prognostic or predictive purpose to thereby prophylactically treat an individual prior to the onset of a disorder characterized by or associated with Tango-77 protein, nucleic acid expression or activity.



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Another aspect of the invention provides methods for determining Tango-77 protein, nucleic acid expression or Tango-77 activity in an individual to thereby select appropriate therapeutic or prophylactic agents for that individual (referred to herein as "pharmacogenomics"). Pharmacogenomics allows for the selection of agents (e.g., drugs) for therapeutic or prophylactic treatment of an individual based on the genotype of the individual (e.g., the genotype of the individual examined to determine the ability of the individual to respond to a particular agent.)

Yet another aspect of the invention pertains to monitoring the influence of agents (e.g., drugs or other compounds) on the expression or activity of Tango-77 in clinical trials.

These and other agents are described in further detail in the following sections.

#### 1. Diagnostic Assays

An exemplary method for detecting the presence or absence of Tango-77 in a biological sample involves obtaining a biological sample from a test subject and contacting the biological sample with a compound or an agent capable of detecting Tango-77 protein or nucleic acid (e.g., mRNA, genomic DNA) that encodes Tango-77 protein such that the presence of Tango-77 is detected in the biological sample. A preferred agent for detecting Tango-77 mRNA or genomic DNA is a labeled nucleic acid probe capable of hybridizing to Tango-77 mRNA or genomic DNA. The nucleic acid probe can be, for example, a full-length Tango-77 nucleic acid, such as the nucleic acid of SEQ ID NO: 1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10 or a portion thereof, such as an oligonucleotide of at least 15, 30, 50, 100, 250 or 500 nucleotides in length and sufficient to specifically hybridize under stringent

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conditions to Tango-77 mRNA or genomic DNA. Other suitable probes for use in the diagnostic assays of the invention are described herein.

A preferred agent for detecting Tango-77 protein is an antibody capable of binding to Tango-77 protein, preferably an antibody with a detectable label. Antibodies can be polyclonal, or more preferably, monoclonal. An intact antibody, or a fragment thereof (e.g., Fab or F(ab')<sub>2</sub>) can be used. The term "labeled", with regard to the probe or antibody, is intended to encompass direct labeling of the probe or antibody by coupling (i.e., physically linking) a detectable substance to the probe or antibody, as well as indirect labeling of the probe or antibody by reactivity with another reagent that is directly labeled. Examples of indirect labeling include detection of a primary antibody using a fluorescently labeled secondary antibody and end-labeling of a DNA probe with biotin such that it can be detected with fluorescently labeled streptavidin. The term "biological sample" is intended to include tissues, cells and biological fluids isolated from a subject, as well as tissues, cells and fluids present within a subject. That is, the detection method of the invention can be used to detect Tango-77 mRNA, protein, or genomic DNA in a biological sample in vitro as well as in vivo. For example, in vitro techniques for detection of Tango-77 mRNA include Northern hybridizations and in situ hybridizations. In vitro techniques for detection of Tango-77 protein include enzyme linked immunosorbent assays (ELISAs), Western blots, immunoprecipitations and immunofluorescence. In vitro techniques for detection of Tango-77 genomic DNA include Southern hybridizations. Furthermore, in vivo techniques for detection of Tango-77 protein include introducing into a subject a labeled anti-Tango-77 antibody. For example, the antibody can be

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labeled with a radioactive marker whose presence and location in a subject can be detected by standard imaging techniques.

In one embodiment, the biological sample contains  
5 protein molecules from the test subject. Alternatively, the biological sample can contain mRNA molecules from the test subject or genomic DNA molecules from the test subject. A preferred biological sample is a peripheral blood leukocyte sample isolated by conventional means  
10 from a subject.

In another embodiment, the methods further involve obtaining a control biological sample from a control subject, contacting the control sample with a compound or agent capable of detecting Tango-77 protein, mRNA, or  
15 genomic DNA, such that the presence of Tango-77 protein, mRNA or genomic DNA is detected in the biological sample, and comparing the presence of Tango-77 protein, mRNA or genomic DNA in the control sample with the presence of Tango-77 protein, mRNA or genomic DNA in the test sample.

20 The invention also encompasses kits for detecting the presence of Tango-77 in a biological sample (a test sample). Such kits can be used to determine if a subject is suffering from or is at increased risk of developing a disorder associated with aberrant expression of Tango-77  
25 (e.g., an immunological disorder). For example, the kit can comprise a labeled compound or agent capable of detecting Tango-77 protein or mRNA in a biological sample and means for determining the amount of Tango-77 in the sample (e.g., an anti-Tango-77 antibody or an  
30 oligonucleotide probe which binds to DNA encoding Tango-77, e.g., SEQ ID NO:1 or SEQ ID NO:3 or SEQ ID NO:6, or SEQ ID NO:10). Kits may also include instruction for observing that the tested subject is suffering from or is at risk of developing a disorder  
35 associated with aberrant expression of Tango-77 if the

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amount of Tango-77 protein or mRNA is above or below a normal level.

For antibody-based kits, the kit may comprise, for example: (1) a first antibody (e.g., attached to a solid support) which binds to Tango-77 protein; and, optionally (2) a second, different antibody which binds to Tango-77 protein or the first antibody and is conjugated to a detectable agent.

For oligonucleotide-based kits, the kit may comprise, for example: (1) an oligonucleotide, e.g., a detectably labelled oligonucleotide, which hybridizes to a Tango-77 nucleic acid sequence or (2) a pair of primers useful for amplifying a Tango-77 nucleic acid molecule;

The kit may also comprise, e.g., a buffering agent, a preservative, or a protein stabilizing agent. The kit may also comprise components necessary for detecting the detectable agent (e.g., an enzyme or a substrate). The kit may also contain a control sample or a series of control samples which can be assayed and compared to the test sample contained. Each component of the kit is usually enclosed within an individual container and all of the various containers are within a single package along with instructions for observing whether the tested subject is suffering from or is at risk of developing a disorder associated with aberrant expression of Tango-77.

## 2. Prognostic Assays

The methods described herein can furthermore be utilized as diagnostic or prognostic assays to identify subjects having or at risk of developing a disease or disorder associated with aberrant Tango-77 expression or activity. For example, the assays described herein, such as the preceding diagnostic assays or the following assays, can be utilized to identify a subject having or

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at risk of developing a disorder associated with aberrant expression or activity. Thus, the present invention provides a method in which a test sample is obtained from a subject and Tango-77 protein or nucleic acid (e.g.,  
5 mRNA, genomic DNA) is detected, wherein the presence of Tango-77 protein or nucleic acid is diagnostic for a subject having or at risk of developing a disease or disorder associated with aberrant Tango-77 expression or activity. As used herein, a "test sample" refers to a  
10 biological sample obtained from a subject of interest. For example, a test sample can be a biological fluid (e.g., serum), cell sample, or tissue.

Furthermore, the prognostic assays described herein can be used to determine whether a subject can be  
15 administered an agent (e.g., an agonist, antagonist, peptidomimetic, protein, peptide, nucleic acid, small molecule, or other drug candidate) to treat a disease or disorder associated with aberrant Tango-77 expression or activity. For example, such methods can be used to  
20 determine whether a subject can be effectively treated with a specific agent or class of agents (e.g., agents of a type which decrease Tango-77 activity). Thus, the present invention provides methods for determining whether a subject can be effectively treated with an  
25 agent for a disorder associated with aberrant Tango-77 expression or activity in which a test sample is obtained and Tango-77 protein or nucleic acid is detected (e.g., wherein the presence of Tango-77 protein or nucleic acid is diagnostic for a subject that can be administered the  
30 agent to treat a disorder associated with aberrant Tango-77 expression or activity).

The methods of the invention can also be used to detect genetic lesions or mutations in a Tango-77 gene, thereby determining if a subject with the lesioned gene  
35 is at risk for a disorder characterized by aberrant

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inflammation. In preferred embodiments, the methods include detecting, in a sample of cells from the subject, the presence or absence of a genetic lesion or mutation characterized by at least one of an alteration affecting  
5 the integrity of a gene encoding a Tango-77-protein, or the mis-expression of the Tango-77 gene. For example, such genetic lesions or mutations can be detected by ascertaining the existence of at least one of: 1) a deletion of one or more nucleotides from a Tango-77 gene;  
10 2) an addition of one or more nucleotides to a Tango-77 gene; 3) a substitution of one or more nucleotides of a Tango-77 gene; 4) a chromosomal rearrangement of a Tango-77 gene; 5) an alteration in the level of a messenger RNA transcript of a Tango-77 gene; 6) an  
15 aberrant modification of a Tango-77 gene, such as of the methylation pattern of the genomic DNA; 7) the presence of a non-wild type splicing pattern of a messenger RNA transcript of a Tango-77 gene; 8) a non-wild type level of a Tango-77-protein; 9) an allelic loss of a Tango-77  
20 gene, and 10) an inappropriate post-translational modification of a Tango-77-protein. As described herein, there are a large number of assay techniques known in the art which can be used for detecting lesions or mutations in a Tango-77 gene. A preferred biological sample is a  
25 peripheral blood leukocyte sample isolated by conventional means from a subject.

In certain embodiments, detection of the lesion involves the use of a probe/primer in a polymerase chain reaction (PCR) (see, e.g., U.S. Patent Nos. 4,683,195 and  
30 4,683,202), such as anchor PCR or RACE PCR, or, alternatively, in a ligation chain reaction (LCR) (see, e.g., Landegran et al. (1988) *Science* 241:1077-1080; and Nakazawa et al. (1994) *Proc. Natl. Acad. Sci. USA* 91:360-364), the latter of which can be particularly useful for  
35 detecting point mutations in the Tango-77-gene (see,

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e.g., Abravaya et al. (1995) *Nucleic Acids Res.* 23:675-682). This method can include the steps of collecting a sample of cells from a patient, isolating nucleic acid (e.g., genomic, mRNA or both) from the cells of the sample, contacting the nucleic acid sample with one or more primers which specifically hybridize to a Tango-77 gene under conditions such that hybridization and amplification of the Tango-77-gene (if present) occurs, and detecting the presence or absence of an amplification product, or detecting the size of the amplification product and comparing the length to a control sample. It is anticipated that PCR and/or LCR may be desirable to use as a preliminary amplification step in conjunction with any of the techniques used for detecting mutations described herein.

Alternative amplification methods include: self sustained sequence replication (Guatelli et al. (1990) *Proc. Natl. Acad. Sci. USA* 87:1874-1878), transcriptional amplification system (Kwoh, et al. (1989) *Proc. Natl. Acad. Sci. USA* 86:1173-1177), Q-Beta Replicase (Lizardi et al. (1988) *Bio/Technology* 6:1197), or any other nucleic acid amplification method, followed by the detection of the amplified molecules using techniques well known to those of skill in the art. These detection schemes are especially useful for the detection of nucleic acid molecules if such molecules are present in very low numbers.

In an alternative embodiment, mutations in a Tango-77 gene from a sample cell can be identified by alterations in restriction enzyme cleavage patterns. For example, sample and control DNA is isolated, amplified (optionally), digested with one or more restriction endonucleases, and fragment length sizes are determined by gel electrophoresis and compared. Differences in fragment length sizes between sample and control DNA

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indicates mutations in the sample DNA. Moreover, the use of sequence specific ribozymes (see, e.g., U.S. Patent No. 5,498,531) can be used to score for the presence of specific mutations by development or loss of a ribozyme cleavage site.

In other embodiments, genetic mutations in Tango-77 can be identified by hybridizing a sample and control nucleic acids, e.g., DNA or RNA, to high density arrays containing hundreds or thousands of oligonucleotide probes (Cronin et al. (1996) *Human Mutation* 7:244-255; Kozal et al. (1996) *Nature Medicine* 2:753-759). For example, genetic mutations in Tango-77 can be identified in two-dimensional arrays containing light-generated DNA probes as described in Cronin et al. supra. Briefly, a first hybridization array of probes can be used to scan through long stretches of DNA in a sample and control to identify base changes between the sequences by making linear arrays of sequential overlapping probes. This step allows the identification of point mutations. This step is followed by a second hybridization array that allows the characterization of specific mutations by using smaller, specialized probe arrays complementary to all variants or mutations detected. Each mutation array is composed of parallel probe sets, one complementary to the wild-type gene and the other complementary to the mutant gene.

In yet another embodiment, any of a variety of sequencing reactions known in the art can be used to directly sequence the Tango-77 gene and detect mutations by comparing the sequence of the sample Tango-77 with the corresponding wild-type (control) sequence. Examples of sequencing reactions include those based on techniques developed by Maxim and Gilbert ((1977) *Proc. Natl. Acad. Sci. USA* 74:560) or Sanger ((1977) *Proc. Natl. Acad. Sci. USA* 74:5463). It is also contemplated that any of a



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variety of automated sequencing procedures can be utilized when performing the diagnostic assays ((1995) *Bio/Techniques* 19:448), including sequencing by mass spectrometry (see, e.g., PCT Publication No. WO 94/16101; 5 Cohen et al. (1996) *Adv. Chromatogr.* 36:127-162; and Griffin et al. (1993) *Appl. Biochem. Biotechnol.* 38:147-159).

Other methods for detecting mutations in the Tango-77 gene include methods in which protection from 10 cleavage agents is used to detect mismatched bases in RNA/RNA or RNA/DNA heteroduplexes (Myers et al. (1985) *Science* 230:1242). In general, the technique of "mismatch cleavage" entails providing heteroduplexes formed by hybridizing (labeled) RNA or DNA containing the 15 wild-type Tango-77 sequence with potentially mutant RNA or DNA obtained from a tissue sample. The double-stranded duplexes are treated with an agent which cleaves single-stranded regions of the duplex such as which will exist due to basepair mismatches between the control and 20 sample strands. RNA/DNA duplexes can be treated with RNase to digest mismatched regions, and DNA/DNA hybrids can be treated with S1 nuclease to digest mismatched regions. In other embodiments, either DNA/DNA or RNA/DNA duplexes can be treated with hydroxylamine or osmium 25 tetroxide and with piperidine in order to digest mismatched regions. After digestion of the mismatched regions, the resulting material is then separated by size on denaturing polyacrylamide gels to determine the site of mutation. See, e.g., Cotton et al. (1988) *Proc. Natl. 30 Acad. Sci. USA* 85:4397; Saleeba et al. (1992) *Methods Enzymol.* 217:286-295. In a preferred embodiment, the control DNA or RNA can be labeled for detection.

In still another embodiment, the mismatch cleavage reaction employs one or more proteins that recognize 35 mismatched base pairs in double-stranded DNA (so called

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"DNA mismatch repair" enzymes) in defined systems for detecting and mapping point mutations in Tango-77 cDNAs obtained from samples of cells. For example, the mutY enzyme of *E. coli* cleaves A at G/A mismatches and the  
5 thymidine DNA glycosylase from HeLa cells cleaves T at G/T mismatches (Hsu et al. (1994) *Carcinogenesis* 15:1657-1662). According to an exemplary embodiment, a probe based on a Tango-77 sequence, e.g., a wild-type Tango-77  
10 sequence, is hybridized to a cDNA or other DNA product from a test cell(s). The duplex is treated with a DNA mismatch repair enzyme, and the cleavage products, if any, can be detected from electrophoresis protocols or the like. See, e.g., U.S. Patent No. 5,459,039.

In other embodiments, alterations in  
15 electrophoretic mobility will be used to identify mutations in Tango-77 genes. For example, single strand conformation polymorphism (SSCP) may be used to detect differences in electrophoretic mobility between mutant and wild type nucleic acids (Orita et al. (1989) *Proc.*  
20 *Natl. Acad. Sci. USA* 86:2766; see also Cotton (1993) *Mutat. Res.* 285:125-144; Hayashi (1992) *Genet Anal Tech Appl* 9:73-79). Single-stranded DNA fragments of sample and control Tango-77 nucleic acids will be denatured and allowed to renature. The secondary structure of single-  
25 stranded nucleic acids varies according to sequence, and the resulting alteration in electrophoretic mobility enables the detection of even a single base change. The DNA fragments may be labeled or detected with labeled probes. The sensitivity of the assay may be enhanced by  
30 using RNA (rather than DNA), in which the secondary structure is more sensitive to a change in sequence. In a preferred embodiment, the subject method utilizes heteroduplex analysis to separate double stranded heteroduplex molecules on the basis of changes in

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electrophoretic mobility (Keen et al. (1991) *Trends Genet* 7:5).

In yet another embodiment, the movement of mutant or wild-type fragments in polyacrylamide gels containing  
5 a gradient of denaturant is assayed using denaturing gradient gel electrophoresis (DGGE) (Myers et al. (1985) *Nature* 313:495). When DGGE is used as the method of analysis, DNA will be modified to insure that it does not completely denature, for example by adding a GC clamp of  
10 approximately 40 bp of high-melting GC-rich DNA by PCR. In a further embodiment, a temperature gradient is used in place of a denaturing gradient to identify differences in the mobility of control and sample DNA (Rosenbaum and Reissner (1987) *Biophys. Chem.* 265:12753).

15 Examples of other techniques for detecting point mutations include, but are not limited to, selective oligonucleotide hybridization, selective amplification, or selective primer extension. For example, oligonucleotide primers may be prepared in which the  
20 known mutation is placed centrally and then hybridized to target DNA under conditions which permit hybridization only if a perfect match is found (Saiki et al. (1986) *Nature* 324:163); Saiki et al. (1989) *Proc. Natl. Acad. Sci. USA* 86:6230). Such allele specific oligonucleotides  
25 are hybridized to PCR amplified target DNA or a number of different mutations when the oligonucleotides are attached to the hybridizing membrane and hybridized with labeled target DNA.

Alternatively, allele specific amplification  
30 technology which depends on selective PCR amplification may be used in conjunction with the instant invention. Oligonucleotides used as primers for specific amplification may carry the mutation of interest in the center of the molecule (so that amplification depends on  
35 differential hybridization) (Gibbs et al. (1989) *Nucleic*

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Acids Res. 17:2437-2448) or at the extreme 3' end of one primer where, under appropriate conditions, mismatch can prevent or reduce polymerase extension (Prossner (1993) Tibtech 11:238). In addition, it may be desirable to  
5 introduce a novel restriction site in the region of the mutation to create cleavage-based detection (Gasparini et al. (1992) Mol. Cell Probes 6:1). It is anticipated that in certain embodiments amplification may also be performed using Taq ligase for amplification (Barany  
10 (1991) Proc. Natl. Acad. Sci USA 88:189). In such cases, ligation will occur only if there is a perfect match at the 3' end of the 5' sequence making it possible to detect the presence of a known mutation at a specific site by looking for the presence or absence of  
15 amplification.

The methods described herein may be performed, for example, by utilizing pre-packaged diagnostic kits comprising at least one probe nucleic acid or antibody reagent described herein, which may be conveniently used,  
20 e.g., in clinical settings to diagnose patients exhibiting symptoms or family history of a disease or illness involving a Tango-77 gene.

Furthermore, any cell type or tissue, preferably peripheral blood leukocytes, in which Tango-77 is  
25 expressed may be utilized in the prognostic assays described herein.

### 3. Pharmacogenomics

Agents, or modulators which have a stimulatory or  
30 inhibitory effect on Tango-77 activity (e.g., Tango-77 gene expression) as identified by a screening assay described herein can be administered to individuals to treat (prophylactically or therapeutically) disorders (e.g., acute or chronic inflammation and asthma)  
35 associated with aberrant Tango-77 activity. In

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conjunction with such treatment, the pharmacogenomics (i.e., the study of the relationship between an individual's genotype and that individual's response to a foreign compound or drug) of the individual may be considered. Differences in metabolism of therapeutics can lead to severe toxicity or therapeutic failure by altering the relation between dose and blood concentration of the pharmacologically active drug. Thus, the pharmacogenomics of the individual permits the selection of effective agents (e.g., drugs) for prophylactic or therapeutic treatments based on a consideration of the individual's genotype. Such pharmacogenomics can further be used to determine appropriate dosages and therapeutic regimens. Accordingly, the activity of Tango-77 protein, expression of Tango-77 nucleic acid, or mutation content of Tango-77 genes in an individual can be determined to thereby select appropriate agent(s) for therapeutic or prophylactic treatment of the individual.

Pharmacogenomics deals with clinically significant hereditary variations in the response to drugs due to altered drug disposition and abnormal action in affected persons. See, e.g., Linder (1997) *Clin. Chem.* 43(2):254-266. In general, two types of pharmacogenetic conditions can be differentiated. Genetic conditions transmitted as a single factor altering the way drugs act on the body are referred to as "altered drug action." Genetic conditions transmitted as single factors altering the way the body acts on drugs are referred to as "altered drug metabolism". These pharmacogenetic conditions can occur either as rare defects or as polymorphisms. For example, glucose-6-phosphate dehydrogenase deficiency (G6PD) is a common inherited enzymopathy in which the main clinical complication is haemolysis after ingestion of oxidant drugs (anti-

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malarials, sulfonamides, analgesics, nitrofurans) and consumption of fava beans.

As an illustrative embodiment, the activity of drug metabolizing enzymes is a major determinant of both the intensity and duration of drug action. The discovery of genetic polymorphisms of drug metabolizing enzymes (e.g., N-acetyltransferase 2 (NAT 2) and cytochrome P450 enzymes CYP2D6 and CYP2C19) has provided an explanation as to why some patients do not obtain the expected drug effects or show exaggerated drug response and serious toxicity after taking the standard and safe dose of a drug. These polymorphisms are expressed in two phenotypes in the population, the extensive metabolizer (EM) and poor metabolizer (PM). The prevalence of PM is different among different populations. For example, the gene coding for CYP2D6 is highly polymorphic and several mutations have been identified in PM, which all lead to the absence of functional CYP2D6. Poor metabolizers of CYP2D6 and CYP2C19 quite frequently experience exaggerated drug response and side effects when they receive standard doses. If a metabolite is the active therapeutic moiety, PM shows no therapeutic response, as demonstrated for the analgesic effect of codeine mediated by its CYP2D6-formed metabolite morphine. The other extreme are the so called ultra-rapid metabolizers who do not respond to standard doses. Recently, the molecular basis of ultra-rapid metabolism has been identified to be due to CYP2D6 gene amplification.

Thus, the activity of Tango-77 protein, expression of Tango-77 nucleic acid, or mutation content of Tango-77 genes in an individual can be determined to thereby select appropriate agent(s) for therapeutic or prophylactic treatment of the individual. In addition, pharmacogenetic studies can be used to apply genotyping of polymorphic alleles encoding drug-metabolizing enzymes

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to the identification of an individual's drug responsiveness phenotype. This knowledge, when applied to dosing or drug selection, can avoid adverse reactions or therapeutic failure and thus enhance therapeutic or prophylactic efficiency when treating a subject with a Tango-77 modulator, such as a modulator identified by one of the exemplary screening assays described herein.

#### 4. Monitoring of Effects During Clinical Trials

Monitoring the influence of agents (e.g., drugs, compounds) on the expression or activity of Tango-77 (e.g., the ability to modulate aberrant inflammation) can be applied not only in basic drug screening, but also in clinical trials. For example, the effectiveness of an agent, as determined by a screening assay as described herein, to increase Tango-77 gene expression, increase protein levels, or upregulate Tango-77 activity, can be monitored in clinical trials of subjects exhibiting decreased Tango-77 gene expression, decreased protein levels, or downregulated Tango-77 activity. Alternatively, the effectiveness of an agent, as determined by a screening assay, to decrease Tango-77 gene expression, decrease protein levels, or downregulate Tango-77 activity, can be monitored in clinical trials of subjects exhibiting increased Tango-77 gene expression, increased protein levels, or upregulated Tango-77 activity.

For example, and not by way of limitation, genes, including Tango-77, that are modulated in cells by treatment with an agent (e.g., compound, drug or small molecule) which modulates Tango-77 activity (e.g., as identified in a screening assay described herein) can be identified. Thus, to study the effect of agents on cellular proliferation disorders, for example, in a clinical trial, cells can be isolated and RNA prepared

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and analyzed for the levels of expression of Tango-77 and other genes implicated in the disorder. The levels of gene expression (i.e., a gene expression pattern) can be quantified by Northern blot analysis or RT-PCR, as described herein, or alternatively by measuring the amount of protein produced, by one of the methods as described herein, or by measuring the levels of activity of Tango-77 or other genes. In this way, the gene expression pattern can serve as a marker, indicative of the physiological response of the cells to the agent. Accordingly, this response state may be determined before, and at various points during, treatment of the individual with the agent.

In a preferred embodiment, the present invention provides a method for monitoring the effectiveness of treatment of a subject with an agent (e.g., an agonist, antagonist, peptidomimetic, protein, peptide, nucleic acid, small molecule, or other drug candidate identified by the screening assays described herein) comprising the steps of (i) obtaining a pre-administration sample from a subject prior to administration of the agent; (ii) detecting the level of expression of a Tango-77 protein, mRNA, or genomic DNA in the preadministration sample; (iii) obtaining one or more post-administration samples from the subject; (iv) detecting the level of expression or activity of the Tango-77 protein, mRNA, or genomic DNA in the post-administration samples; (v) comparing the level of expression or activity of the Tango-77 protein, mRNA, or genomic DNA in the pre-administration sample with the Tango-77 protein, mRNA, or genomic DNA in the post administration sample or samples; and (vi) altering the administration of the agent to the subject accordingly. For example, increased administration of the agent may be desirable to increase the expression or activity of Tango-77 to higher levels than detected,



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i.e., to increase the effectiveness of the agent.  
Alternatively, decreased administration of the agent may  
be desirable to decrease expression or activity of  
Tango-77 to lower levels than detected, i.e., to decrease  
5 the effectiveness of the agent.

### C. Methods of Treatment

The present invention provides for both  
prophylactic and therapeutic methods of treating a  
subject at risk of (or susceptible to) developing or  
10 having a disorder associated with aberrant Tango-77  
expression or activity. Alternatively, disorders  
associated with aberrant IL-1 production can be treated  
with Tango-77. Such disorders include acute and chronic  
inflammation, asthma, some classes of arthritis,  
15 autoimmune diabetes, systemic lupus erythematosus and  
inflammatory bowel disease.

#### 1. Prophylactic Methods

In one aspect, the invention provides a method for  
preventing in a subject, a disease or condition  
20 associated with an aberrant Tango-77 expression or  
activity (or aberrant IL-1 expression or activity), by  
administering to the subject an agent which modulates  
Tango-77 expression or at least one Tango-77 activity.  
Subjects at risk for a disease which is caused or  
25 contributed to by aberrant Tango-77 expression or  
activity can be identified by, for example, any or a  
combination of diagnostic or prognostic assays as  
described herein. Administration of a prophylactic agent  
can occur prior to the manifestation of symptoms  
30 characteristic of the Tango-77 aberrancy, such that a  
disease or disorder is prevented or, alternatively,  
delayed in its progression. Depending on the type of  
Tango-77 aberrancy, for example, a Tango-77 agonist or  
Tango-77 antagonist agent can be used for treating the

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subject. The appropriate agent can be determined based on screening assays described herein.

## 2. Therapeutic Methods

Another aspect of the invention pertains to methods of modulating Tango-77 expression or activity for therapeutic purposes. The modulatory method of the invention involves contacting a cell with an agent that modulates one or more of the activities of Tango-77 protein activity associated with the cell. An agent that modulates Tango-77 protein activity can be an agent as described herein, such as a nucleic acid or a protein, a naturally-occurring cognate ligand of a Tango-77 protein, a peptide, a Tango-77 peptidomimetic, or other small molecule. In one embodiment, the agent stimulates one or more of the biological activities of Tango-77 protein. Examples of such stimulatory agents include active Tango-77 protein and a nucleic acid molecule encoding Tango-77 that has been introduced into the cell. In another embodiment, the agent inhibits one or more of the biological activities of Tango-77 protein. Examples of such inhibitory agents include antisense Tango-77 nucleic acid molecules and anti-Tango-77 antibodies. These modulatory methods can be performed *in vitro* (e.g., by culturing the cell with the agent) or, alternatively, *in vivo* (e.g., by administering the agent to a subject). As such, the present invention provides methods of treating an individual afflicted with a disease or disorder characterized by aberrant expression or activity of a Tango-77 protein or nucleic acid molecule. In one embodiment, the method involves administering an agent (e.g., an agent identified by a screening assay described herein), or combination of agents that modulates (e.g., upregulates or downregulates) Tango-77 expression or activity. In another embodiment, the method involves

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administering a Tango-77 protein or nucleic acid molecule as therapy to compensate for reduced or aberrant Tango-77 expression or activity.

Stimulation of Tango-77 activity is desirable in situations in which Tango-77 is abnormally downregulated and/or in which increased Tango-77 activity is likely to have a beneficial effect. Conversely, inhibition of Tango-77 activity is desirable in situations in which Tango-77 is abnormally upregulated and/or in which decreased Tango-77 activity is likely to have a beneficial effect.

This invention is further illustrated by the following examples which should not be construed as limiting. The contents of all references, patents and published patent applications cited throughout this application are hereby incorporated by reference.

#### EXAMPLES

##### Example 1: Isolation and Characterization of Human Tango-77 cDNAs

Cytokine genes IL-1 $\alpha$ , IL-1 $\beta$  and IL-1ra have been found to be closely clustered on chromosome 2, i.e., IL-1 $\alpha$ , IL-1 $\beta$  and IL-1ra are located within 450 kb of each other. BAC clones containing IL-1 $\alpha$  and IL-1 $\beta$  were used to identify other proximal unknown cytokine genes. To do this, a BAC clone containing IL-1 $\alpha$  and IL-1 $\beta$  was selected from a BAC library (Research Genetics, Huntsville, Alabama) using specific primers designed against IL-1 $\alpha$  and IL-1 $\beta$ . The DNA from the BAC was extracted and used to make a random-sheared genomic library. From this BAC library, 4000 clones were selected for sequencing. The resulting genomic sequences were then assembled into contigs and used to screen proprietary and public data bases. One genomic contig was found to contain two

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segments of sequences which resemble IL-1ra. These two segments are potential exons of Tango-77 gene.

Two PCR primers were then designed from the two potential exons and used to screen a panel of cDNA libraries for the expression of a Tango-77 message. A cDNA library from TNF- $\alpha$  treated human lung epithelia showed a positive band of the predicted size (i.e., if the two exons are spliced together). Using the PCR fragment as a probe, a single cDNA clone was isolated from the same library. This cDNA contains an insert of 989 bp. The cDNA clone contains three possible open reading frames. The first open reading frame encompasses 534 nucleotides (nucleotides 356-889 of SEQ ID NO:1; SEQ ID NO:3) and encodes a 178 amino acid protein (SEQ ID NO:2). This protein may include a predicted signal sequence of about 63 amino acids (from amino acid 1 to about amino acid 63 of SEQ ID NO:2 (SEQ ID NO:4)) and a predicted mature protein of about 115 amino acids (from about amino acid 64 to amino acid 178 of SEQ ID NO:2 (SEQ ID NO:5)).

The second putative nucleotide open reading frame encompasses 498 nucleotides (nucleotides 389-889 of SEQ ID NO:1; SEQ ID NO:6) and encodes a 167 amino acid protein (SEQ ID NO:7). This protein includes a predicted signal sequence of about 52 amino acids (from amino acid 1 to about amino acid 52 of SEQ ID NO:7 (SEQ ID NO:8)) and a predicted mature protein of about 115 amino acids (from about amino acid 53 to amino acid 167 of SEQ ID NO:7 (SEQ ID NO:9)).

The third open reading frame (nucleotides 372-889 of SEQ ID NO:1; SEQ ID NO:10) encompasses 408 nucleotides and encodes a 136 amino acid protein (SEQ ID NO:11). This protein includes a predicted signal sequence of about 21 amino acids (from amino acid 1 to about amino acid 21 of SEQ ID NO:11 (SEQ ID NO:12)) and a predicted

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mature protein of about 115 amino acids (from about amino acid 22 to amino acid 136 of SEQ ID NO:11 (SEQ ID NO:13)).

Tango-77 is predicted to be 35% identical to human IL-1ra at the amino acid level.

Example 2: Expression of Tango-77 mRNA in Human Tissues

The expression of Tango-77 was analyzed using Northern blot hybridization. A PCR generated 989 bp Tango-77 product was radioactively labeled with <sup>32</sup>P-dCTP using the Prime-It kit (Stratagene; La Jolla, CA) according to the instructions of the supplier. Filters containing human mRNA (MTNI and MTNII: Clontech; Palo Alto, CA) were probed in ExpressHyb hybridization solution (Clontech) and washed at high stringency according to manufacturer's recommendations.

Tango-77 mRNA was not detected in any unstimulated tissues (brain, liver, spleen, skeletal muscle, testis, pancreas, heart, kidney and peripheral blood leukocytes) mRNA on Clontech Northern blots.

Over 96 cDNA libraries were then tested for the presence of Tango-77 using PCR amplification. Only three libraries displayed a positive signal. These libraries were the TNF $\alpha$ -treated bronchoepithelium, TNF $\alpha$ -treated SSC cell line and anti-CD3-treated T cells.

Example 3: Characterization of Tango-77 Proteins

In this example, the predicted amino acid sequence of human Tango-77 protein was compared to the amino acid sequence of known protein IL-1ra. In addition, the molecular weight of the human Tango-77 proteins was predicted.

The human Tango-77 cDNA (Figure 1; SEQ ID NO:1) isolated as described above encodes a 178 amino acid protein (Figure 1; SEQ ID NO:2) or a 167 amino acid

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protein (Figure 1; SEQ ID NO:7) or a 136 amino acid protein (Figure 1; SEQ ID NO:11). The signal peptide prediction program SIGNALP Optimized Tool (Nielsen et al. (1997) *Protein Engineering* 10:1-6) predicted that

5 Tango-77 includes a 63 amino acid signal peptide (amino acid 1 to about amino acid 63 of SEQ ID NO:2 (SEQ ID NO:4)) preceding the 115 mature protein; or preceding the 115 mature protein (about amino acid 52 to amino acid 167 of SEQ ID NO:7 (SEQ ID NO:8)); or preceding the 115

10 mature protein (about amino acid 21 to amino acid 136 of SEQ ID NO:11;SEQ ID NO:12).

As shown in Figure 2, Tango-77 has a region of homology to IL-1ra (SEQ ID NO:14).

Mature Tango-77 has a predicted MW of about 13 kDa

15 and the predicted MW for the immature Tango-77 is 19.6 kDa, 18.5 kDa or 15.2 kDa, not including post-translational modifications.

#### Example 4: Preparation of Tango-77 Proteins

Recombinant Tango-77 can be produced in a variety

20 of expression systems. For example, the mature Tango-77 peptide can be expressed as a recombinant glutathione-S-transferase (GST) fusion protein in *E. coli* and the fusion protein can be isolated and characterized. Specifically, as described above, Tango-77 can be fused

25 to GST and this fusion protein can be expressed in *E. coli* strain PEB199. Expression of the GST-Tango-77 fusion protein in PEB199 can be induced with IPTG. The recombinant fusion protein can be purified from crude bacterial lysates of the induced PEB199 strain by

30 affinity chromatography on glutathione beads.

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Example 5: Alternatively spliced forms of IL-1ra and  
Tango-77

Computer program Procrustes (Gelfand et al., 1996, *Proc. Natl. Acad. Sci. USA*, 93:9061-9066) is an alignment  
5 algorithm that predicts the presence of alternatively  
spliced exons for a protein of interest in a stretch of  
genomic DNA. Using the IL-1ra sequence, Procrustes was  
used to search for the presence of additional sequences  
that might encode for alternatively spliced forms of IL-  
10 1ra in the two overlapping BAC genomic sequences (see  
Fig. 3 and Fig. 4). Potential sequences that encode  
variant exons for IL-1ra were identified. These  
predicted exons aligned well with the N-terminal region  
of IL-1ra, but were not present in Tango-77. The results  
15 from Procrustes predicts the existence of more spliced  
forms of IL-1ra.

Furthermore, Procrustes also predicted an  
additional sequence in BAC1 and BAC2 that encodes an  
alternatively spliced exon for Tango-77 (T77-procrustes;  
20 Fig. 5). This predicted splice variant form of Tango-77,  
T77-procrustes, was aligned with Tango-77 (Fig. 6) and  
with IL-1ra and IL-1 $\beta$  (Fig.7).

PCR primers within this sequence can be used to  
generate a product that can be used to screen a panel of  
25 cDNA libraries using standard techniques. Suitable cDNA  
libraries include libraries made from TNF $\alpha$ -treated  
bronchoepithelium, TNF $\alpha$ -treated SSC cell line and anti-  
CD3-treated T cells. The resulting cDNA clone(s) can be  
isolated from the library and sequenced to identify  
30 additional Tango-77 cDNAs.

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Equivalents

Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, many equivalents to the specific  
s embodiments of the invention described herein. Such equivalents are intended to be encompassed by the following claims.



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What is claimed is:

1. An isolated nucleic acid molecule selected from the group consisting of:

- a) a nucleic acid molecule comprising a  
5 nucleotide sequence which is at least 45% identical to the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807, or a complement thereof;
- 10 b) a nucleic acid molecule comprising a fragment of at least 300 nucleotides of the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807, or a complement thereof;
- 15 c) nucleic acid molecule which encodes a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or an amino acid sequence encoded by the cDNA insert of the  
20 plasmid deposited with ATCC as Accession Number 98807;
- d) a nucleic acid molecule which encodes a fragment of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID  
25 NO:12, SEQ ID NO:13, wherein the fragment comprises at least 15 contiguous amino acids of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or the polypeptide encoded by the cDNA insert of the plasmid  
30 deposited with ATCC as Accession Number 98807; and
- e) a nucleic acid molecule which encodes a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9,

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SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or an amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807, wherein the nucleic acid molecule hybridizes to a nucleic acid molecule comprising SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, or the complement thereof under stringent conditions.

2. The isolated nucleic acid molecule of claim 1, which is selected from the group consisting of:

10 a) a nucleic acid comprising the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, or SEQ ID NO:10 or the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807, or a complement thereof; and

15 b) a nucleic acid molecule which encodes a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or an amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807.

3. The nucleic acid molecule of claim 1 further comprising vector nucleic acid sequences.

4. The nucleic acid molecule of claim 1 further comprising nucleic acid sequences encoding a heterologous polypeptide.

5. A host cell containing the nucleic acid molecule of claim 1.

6. The host cell of claim 5 which is a mammalian host cell.

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7. A non-human mammalian host cell containing the nucleic acid molecule of claim 1.

8. An isolated polypeptide selected from the group consisting of:

5 a) a fragment of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, wherein the fragment comprises at least 15 contiguous amino acids of SEQ ID  
10 NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, or SEQ ID NO:13.

b) a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8,  
15 SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or an amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807, wherein the polypeptide is encoded by a nucleic acid molecule which hybridizes to a nucleic acid molecule  
20 comprising SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10 or the complement thereof under stringent conditions;

c) a polypeptide which is encoded by a nucleic acid molecule comprising a nucleotide sequence which is  
25 at least 55% identical to a nucleic acid comprising the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, or SEQ ID NO:10.

9. The isolated polypeptide of claim 8 comprising the amino acid sequence of SEQ ID NO:2, SEQ ID  
30 NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or an amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807.

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10. The polypeptide of claim 8 further comprising heterologous amino acid sequences.

11. An antibody which selectively binds to a polypeptide of claim 8.

5 12. A method for producing a polypeptide selected from the group consisting of:

a) a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID  
10 NO:12, SEQ ID NO:13, or an amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807;

b) a fragment of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID  
15 NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or an amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807, wherein the fragment comprises at least 15 contiguous amino acids  
20 of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or an amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807; and

25 c) a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or  
30 an amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807, wherein the polypeptide is encoded by a nucleic acid molecule which hybridizes to a nucleic acid sequence of

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SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, or SEQ ID NO:10  
under stringent conditions;

comprising culturing the host cell of claim 5  
under conditions in which the nucleic acid molecule is  
5 expressed.

13. A method for detecting the presence of a  
polypeptide of claim 8 in a sample, comprising:

- a) contacting the sample with a compound which  
selectively binds to a polypeptide of claim 8; and
- 10 b) determining whether the compound binds to the  
polypeptide in the sample.

14. The method of claim 13, wherein the compound  
which binds to the polypeptide is an antibody.

15 15. A kit comprising a compound which selectively  
binds to a polypeptide of claim 8 and instructions for  
use.

16. A method for detecting the presence of a  
nucleic acid molecule of claim 1 in a sample, comprising  
the steps of:

- 20 a) contacting the sample with a nucleic acid  
probe or primer which selectively hybridizes to the  
nucleic acid molecule; and
- b) determining whether the nucleic acid probe or  
primer binds to a nucleic acid molecule in the sample.

25 17. The method of claim 16, wherein the sample  
comprises mRNA molecules and is contacted with a nucleic  
acid probe.

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18. A kit comprising a compound which selectively hybridizes to a nucleic acid molecule of claim 1 and instructions for use.

19. A method for identifying a compound which  
5 binds to a polypeptide of claim 8 comprising the steps of:

- a) contacting a polypeptide, or a cell expressing a polypeptide of claim 8 with a test compound; and
- 10 b) determining whether the polypeptide binds to the test compound.

20. The method of claim 19, wherein the binding of the test compound to the polypeptide is detected by a method selected from the group consisting of:

- 15 a) detection of binding by direct detecting of test compound/polypeptide binding;
- b) detection of binding using a competition binding assay; and
- c) detection of binding using an assay for  
20 Tango-77-mediated signal transduction.s

21. A method for modulating the activity of a polypeptide of claim 8 comprising contacting a polypeptide or a cell expressing a polypeptide of claim 8 with a compound which binds to the polypeptide in a  
25 sufficient concentration to modulate the activity of the polypeptide.

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22. A method for identifying a compound which modulates the activity of a polypeptide of claim 8, comprising:

- a) contacting a polypeptide of claim 8 with a  
5 test compound; and
- b) determining the effect of the test compound on the activity of the polypeptide to thereby identify a compound which modulates the activity of the polypeptide.

GTGGACCCACGGCTCCGCAGACGTCTACCTGGGGGTCCCGTCTGCGCTCCCGGGATGGAACGCCAGGGGAACTTA 79  
 GGCAGGCGAGCGGACGGGCACCTCCCGCGGGACGAACCTCACTCGGTGGCCCTCCTACTTCCCGGGCCGTGTTCCAACGCC 158  
 TGAGAATAACGGGAACAGCGGTCTACTACCGACAGCGGCAGCAGCGGCCTCTCTCAATTGGGCAAAGCACTCCAGAC 237  
 TTTTGGGAAGAGTGACACCAAAGGCAAGCACCTGCTTGGCAGGCCCTCAGCTTCTACGCAAGTATAAGTCTTGGACTT 316  
 CATTCCATTTTCTGTTGAGTAATAAACTCAACGTTGAAA M S F V G E N S G V 10  
 ATG TCC TTT GTG GGG GAG AAC TCA GGA GTG 385  
 K M G S E D W E K D E P Q C C L E D P A 30  
 AAA ATG GGC TGT GAG GAC TGG GAA AAA GAT GAA CCC CAG TGC TGC TTA GAA GAC CCG GCT 445  
 G S P L E P G P S L P T M N F V H T K I 50  
 GGA AGC CCC CTG GAA CCA GGC CCA AGC CTC CCC ACC ATG AAT TTT GTT CAC ACA AAG ATC 505  
 F F A L A S S L S S A S A E K G S P I L 70  
 TTC TTT GCA TTA GCC TCA TCC TTG AGC TCA GCC TCT GCG GAG AAA GGA AGT CCG ATT CTC 565  
 L G V S K G E F C L Y C D K D K G Q S H 90  
 CTG GGG GTC TGT AAA GGG GAG TTT TGT CTC TAC TGT GAC AAG GAT AAA GGA CAA AGT CAT 625  
 P S L Q L K K E K L M K L A A Q K E S A 110  
 TCA TCC CTT CAG CTG AAG AAG GAG AAA CTG ATG AAG CTG GCT GCC CAA AAG GAA TCA GCA 685  
 R R P F I F Y R A Q Y G S W N M L E S A 130  
 CGC CCG CCC TTC ATC TTT TAT AGG GCT CAG GTG GGC TCC TGG AAC ATG CTG GAG TCG GCG 745  
 A H P G W F I C T S C N C N E P V G V T 150  
 GCT CAC CCC GGA TGG TTC ATC TGC ACC TCC TGC AAT TGT AAT GAG CCT GTT GGG GTG ACA 805  
 D K F E N R K H I E F S F Q P V C K A E 170  
 GAT AAA TTT GAG AAC AGG AAA CAC ATT GAA TTT TCA TTT CAA CCA GTT TGC AAA GCT GAA 865  
 M S P S E V S D \* 179  
 ATG AGC CCC AGT GAG GTC AGC GAT TAG 892  
 GAAACTGCCCCATTGAACGCCCTTCTCGCTAATTTGAACTAATTGTATAAAAAACACCAAACCTGCTCACTAAAAAAA 971  
 AAAAAAAGGGCGGCCGC 989

Fig. 1



1  
 IL1ra-human 50  
 MEICRGLRSH LITLLFLFH SETICRPSGR KSSKMQAFRI WDVNQKTFYL  
 T77-human  
 IL1b-human  
 Consensus  
 51  
 IL1ra-human 100  
 RNNQLVAGYL QGPNVNLEEK IDVVFIEPH. ALFLGIHGK MCLSCVKSGD  
 T77-human  
 IL1b-human  
 Consensus  
 101  
 IL1ra-human 150  
 ETR..LQLEA VNITDLSENR KQDKR.FAFI RSDSGPTTSF ESAACPGWFL  
 T77-human  
 IL1b-human  
 Consensus  
 151  
 IL1ra-human 192  
 CTAMEADQPV SLTNMPDEGV MVTKFYFQED E-  
 T77-human  
 IL1b-human  
 Consensus

FIG. 2

>Contig1  
GAAGTGAAGATATAATGTATAGTAGTAATATATAATGTTAGGTGAATTAA  
AGGAAATAGAAATATATTGGGGAGTAATTATGGGTGTAAAGAAATATAGTA  
GGGAAGTATTTAGATTTGAGAAAAAAGGAATTTAGTGTAGGTGAA  
NAATAAAAGNANAAGGTTAAAAATTAAAAAAATTAATATAAAATAAAT  
AAATAAAATAAAAAATAAAATAAAAAATTTAAAAAATTAAAAAATATAA  
AAAAATAAGAAATGGAAGTGGATTCTTAGAAAAAAGAAAGTAAGGTGA  
TATGAGGAGATAGAGAGGATGTGGTGTGAGATGATTGGTTTAATTAGAAA  
ATAGGTTTTGAATAGAGTGGGAAAGTAGAGTTTGGTAAATGTGGGGGGA  
AGAGGGTAATGTTGTTTGAAGTGAAGAAAAAATGGTATATTTTATAAAA  
TAATGAGGAAAGTGTGTGAAAAAAATTTGGGGATTGGGAAGGTGAT  
ATATAAAGTTGTGGAAAAATTTGGGGGTGGGGTTTATTAGGATTAAAAA  
GTTATTTAAAGAATGAAAATGAATTTTGTGTTGTAATTTGGGGATAAGAA  
ATTAATGTTTAGAAAGAAAGGGAATAATTGAAGAAAAAATTTAGATTT  
TGGAATTTAAAAATATTGTGGGTGTAAATAGGAAGGATTTTAAAGGTA  
ATTGTGGAAGGATTGTGTGGAAAAATAATAGGGAGAAAAATGGGG  
>Contig2  
GCATCTAACTGGAGCCTGCATTATTACAGATTTAGCATCACCAAAGTCTA  
AACAAATTAGACTGACTAAGGCAGAACTGCCCTTATGACAGCAGACATAAG  
AAGGAAAAGGCCAAAACACTGTGTTAAAAATTATCCAAATGTGAGGAAAA  
GGCAAAGAGAGTAGGTGTGCCTTTTGTGTCTAAGCTGCCTGCCCAAGG  
GGCATCTGATGCTCTCAGGCAGGAGTCCACAAATTTTGTAAAAGA  
TCAGATAGTAAATCTTTTCAGCGTGAAGAGCATGAGGTCTCTGTACAAA  
TACTCAACCACCATTACAACATGAAAGCAGCCAACAGACAACACATGACA  
AATGAGTGTGGCTGTGTTCCAGTAAATCTTGATTACAAAAACAGGCAAGA  
GGCCAGAGCTGACCCATGGGCCATAGTTTGTGACCCCTTCTGTAAAGGA  
AAGTATTTTGTGTTGACTTGCTGTTTACCATTGATTGAACACAAGGCTCT  
GTAAAGTTACTTGTAACTTGCAGAAGATTGATGAGTGGCAAGTAATTTT  
TATTCACCAGAATATAAAATTATTTCTGTTTCAGTAGAAAAGATAAACCAA  
CTGTGATATTATGGTCCTG  
>Contig3  
GGGGTGTCTGTCTACCATGTGCTCGCAGTTCTGTAATAAATGTTCTCTCA  
AGATCCTTAAAAATCTCTTGGAAATTATAAAAAATATTGGAAAGAGAAGAAC  
AGTTTTTAAATATATATATATATATATATTTTTTTTGGAGATGGAGTCTT  
GCTCTGTGCTCCAGGCTGGAGTGCAGTGGCGCAAACCTTGGTTCACCACAA  
CCTCTGCCTCCCGGGTTCAGCGATTCTTCTGCCTCAGCCTCCTGAGTAG  
CTGGGACTACAGGCGCCCGCCACCAGCCAGCTAATTTTTGTATTTTTTA  
GTAGAGACGAGGTTTTACTATGTTGGCTAGGCTGGTCTCAAACCTCCTGAC  
CTTGATGATCTGCCCGCTTGGCCTCCCAAAGTGTGGGATTACAGGTGTG  
AGCCACTGCACCTGGCCAGTTTTTTAAATATATTTTTTAAAAACACTTGAA  
TAAGAGTCAGTGTAAGTCTAGAAAGTTTAAAAATGCTTCACAGAACCCAG  
GGTTTACATTCAAGATTCTCACAACAAACCTATTGTAAAGGTGAGTAAG  
GCATGTTATTACAGAGAAAAAGTTTGGGAGCAAACTGTAAAAAATTATAT  
TTTTGTTGATTTTTCTAAGAGAAAGAGTATTGTTATGTTCTCTAACCTC  
TGTTGATTACTACTTTAAGTGATTTCTTGGAGGCATGATGATCC  
>Contig4  
GCCGTTTCATAGAAAACCTGAAAGCAATAAGATGACTAGGTAAGCATGACAT  
TTAAAAGGTATTCATGGGACGTGGTTACAAAACCAACTCACAACATAAAA  
GTCTTAGGACCTCTCGCTGACTTAGGAGCCTGATCCCAACTCTGAGAATG  
ACTCAGTGTGTTACCCTGTGGCTAGTGTAGACCAATGATCCTGTCTCAGA  
GTCAC TAGCCAACAGCCCATATCAAGTACTTGAAACTTTGACTCAGAAAC  
CTCAGTGTGAGAACCTTTGACCTAGGAACCCACCTGTAGTGGTTAACTGCA  
ATTTGCACCCCTTAGTTGAGGCTTTACAACACCGGGGGCGGGGAGGGGA  
AAGGCATANANCTGATGACCTAAAGGAAACCCATTGCAGCAACGCTTTTG  
TGTTAAGTGTAATAAAGTGTGTTTGTAGAACTCTCCAGGTAATGCCTT  
TGTTATTTAATGTGTCTGAGACAATTCTGCACATTAAAGAAATAAAAAA  
TTACCTTTGAATTTCAATTTGAAATGTGTAATTGACATTAGACTTCTATT  
TGAATTTGAAATGTCTAAACAATGTGGTTAAGTTTGTAAAAGGTGTGTG  
AATTTTGAAGTCTGATTTACTACATTTTTTTTAAATTTCTTTTTTTTGG  
AGTTTTAGGGATTGCTTAGATGGCTAGAAAGATTTTATTCATCAGATTTT

FIG. 3 (1 of 52)

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TAAGTCTGCCCTTGGCAGGCACCTTGACAG. JTTTGAAAGAATCAGATATATC  
AAATTTGTAGTTTAAAAATATTTAAGGGAACCTCAATTAACCTATGCTAGAAA  
AGAGAATTAAGTATTTAGGAGGATTTAATATGGTGTGAAAGTTGTGAAAA  
TCAAATGGAGACACTAATGTTAAGAAAACCTGATAAATGGAACCAGGG  
AAAGGCATGAAGATAGAGTTCTCACACTTGTATCCCTGATCATGAAAAAG  
ATCTGC

>Contig5

GGGTTTTTCCGCGTTTTTACCCGAAATCTTCAAGGGATGGGAAAAAGAAA  
ATTGCTAAAAAATCTCGGTTTTTTGGTTTTTAACAGATATTTACACNTGG  
ATCCCATTTATTATGTGTGTCCCAAGGTTTTTCGGTGGGTTCCCAATCAGT  
TAGCCCCCTCCACAGTGAAAGCACTTTACTTTATCACCTTCACCTAAAG  
CATAAAATCCAGCTCTTGAAAGCTGCTCCTTGTTAACTGAATATATCCAC  
ATCCCAAAAGTAATGATCCATGCTTCATAATCTGCCACGGATGGATGGAT  
GGATGGATGGATGGATGGATGGATGGATGAATGGATGGATTGATTTCTTG  
GAGGATTTGTTGAATTTGGGAAATTCACGCCAGGACAGCTGGCCCAAAC  
TGCCCGCGACAATCTGCTCGGTACAAGGGGAGGGTCTTGAGAGGGGTGCG  
GCCCGAGCCCCAGTTTGGAAATGCCAATTGGCTCTGCAGCCGGGCCTTA  
GCCACTTGGGTCTGGCGTCCCTCCATTATTAGCGCCATGCCGGCTCGGG  
TGCTGCCAAGTCCCTGAGAGCACAAAGCC

>Contig6

CGCGCTCAAGAAAAGCTGAAGTGTGAATGTTCTGTCTACCTTCACAGTAA  
ATGCTAAGAGAATGACCCAGAGCAGAGGGTATCACTCTGCTACGGAGGA  
TTGATTGTAAGTGGCTCTCCTGCCCTTAGCAAGAAATGCCAGAACCATGGT  
CATTCAAGTCTTGACCAAAACTGCCTTCATGAGAATCAACTTCCCCAA  
GAAAAAAAAGCAGAAACAGGCAAGCTTCCAGCATGGTAGGTAATACTG  
ACCTTCTTCCCTCCTTCTTGGAGATTACACAGTAATAATGCATAAA  
GCTTTGCCAATGGAATAAGCACTGCCAGGGGTTTTTGTCTGCCTGGAC  
TGAAATGCTCTTTTTGCGTTATCATAGAATCCAGTGCAGTCTGAGTAGA  
CTCTAAGCAAAAGGGACATTTTTCAAAAAGGCTTTAAATTGCTAGTACAA  
AGAAGGCAACAAAACCTTGGCTAAGTGTGGACAGATTAACCTCACTTGGTGT  
TTTGGCTCTTCAGTTTTCCCTTGGCTGCGAAGTACTCCTGAAGCTTTCTC  
TGCGGCTCTTCTGCAAGCAGGCAAGCAAAAAACGACTGAACCTTTATTT  
CGAGAT

>Contig7

GAAGAGCCGCTAACTTGCTGTAGTGATAAGGAATGAACTAAGGCTAGGGA  
CATATTAACATCCGCTGGTGGTGACTCTTTAGCCTAGATCTTACCCCACT  
CCTGCTCCTTCCATATGGTTCGGTCTCAGGCTCACTACCGATCAATGGCG  
TACTAAAAGCACTAACTATAGACTCCAACACGTCTGTCTGTGTTTACG  
ACAAGCCCTGGAGTTAATCCCTCTGACAGTAGCTCAGATAAGGATGGGCT  
ATCATGGGGCCCGAACTGGGGCATGACGCTCGTCACCAACGCATGAGCTC  
CCCAAGTATGCTATACCTGTCCCTATGAAGGGCTTCCAACCTCTATGTGCA  
GTCCCCATGTGGAGAGTCAGGTATTGATTGATCAAGCCAGGGGTGTGGTG  
AATGGGGAGCTTCTACAGGGGTAATGATAATTGAAATGCACGGTGATGG  
GGATTTTCATATTGGTCTCCTAAGGAGATAACAGATTGGATGCGGGGTCC  
ATATTCCACTGCCAGGGTGTGTACCGAGGGTATCTGCAGGTGGATCTCC  
TCCCCACGTTTGATTAATACTCCTGTCTTGGGAAGCATAGACGGGCGGG  
GAAATGATGAAGGTGACCACTCCCC

>Contig8

GGGAACGCAGTGCTCTGTACGATGGCCTTGATTGCGAATTCCTGCAGGGG  
GGG

>Contig9

GGCAAGAGATTTAATATTCAATCCATCTTCATTTGGAAGATGAAAAATTG  
GGGACCAGAGAGGGGAGGGGACTGGGCCAAGTTTTCAAGAAAAGTCAGT  
AGGAATTGTGAATTCCTGGGGGCCGGGGCCATTAGTGCTGTTTTGGATC  
AGTAAATGGAGATGTGAGTTTCAACAGTAACAGGGACATTTTAAATTA  
AATGATTAACTTTAGAAAATGTCCTATTTTGTAAATAATGATGGATTCA  
CAGGAAGGTACAAAGAAATGTCCAGAGAGTTCNTGAGCCCCCTTCAGCCA  
GCTTCTTCCAATGTTAACATCTTGCAATTATTATAGTACAACATCAAACT  
GGGAAATC3ATATTGGTACTGTCCAGATAGCTTACTCAGATTTTGCCAGT  
TATACTTCCACTCATTTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTG

FIG. 3 (2 of 52)

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TGTGTGTAGCTCTATGCAATTTTATG1...GTAGCTTCATGTAAGCACC...  
AATCACAATACTTAACCTATGCCCTCATCAAGACTCTCTCTTGCTATGC  
TTTACAGCTGTATCCTCTTCATCTCCAAACCCTAAGCCCACCTCACCGCC  
TCCACCATCTCTAATCCCTGGCAACCACTATTCTGTGCTCCATCTCTGTA  
ATTAATTGTGTTAATTAATGTTATACAAATGGAATCATGAAGTATGTGTC  
CTTTGAGATTGGGCTGTTAATTTTCACTCAGCACAATTTCCGTGAGTCT  
AATCCAACCTGTGTGTAGCAGTAATTTCTTCTTATTATTGCTGAATAAT  
ATGCCATGGTATGGATGTATCACAGTGTGTCTAATCCTTTGCCATTGAA  
AGGAATTTGGATAATTTCCAGGTTTTGGCTATTATGAATAAAGTGAACAT  
AAGACATGTGTGTACAAATTTTGGTGTGATCAAAAGTCTCATTCTCTGG  
GATAAATGCCCGGTAATGAAATGGCTGGGTTGTGTGGG

>Contig10

GCAAGAACACAGGCGCGTATTATAACCTTACTACCAAGACCTGAACCCAT  
ATAAAGGTTTATGCGTAACAATCATCATCCCTGTTCCAGAAGATTACACG  
TACGACCACGCTGGCTCACCAGCTCACGTGGGCCAGTACCAGAAATTCT  
CCCAAACAAACAGTCGTGTCTGAAAACAATCGCGGTGACCTCCACGGTTA  
GAAAAGCCTGTTTTCAAGTCCTGGAATTGCCACATATTAGCTGGGTAAT  
TTGGGCATCACATTTACTCTCTCCGAATTTGAGATTGCAAAAACCTCATTG  
GATTGTTTTGTGGATTGAAAGAAATAATGTAAATTTAGGCCGAGTGCTTT  
GACTTACGCTGTAACTCTATCACTTTGGGAGGCCAAAGCAGGAGGGTCA  
CTTGAGCTCAGGAATTTGAGACCACCTCTGGCAACATAGTGAGATCCTGT  
CTCTACAAAAAATTTTTTTTAAATTATCCAGCATGGTGGTACACGCCTGT  
ATTTCCAGCTACTCAGGAGACTGAGGTGTGAGGATTGCTAGAACCCTGGGA  
GATCAAGTCAACAGTGAGCCGTGGTTGTGCCACTGCCCTCCAACCTCAGT  
GACAGAGGAAGACCCTGTCTCAAAAAAAAAAAAAAAAAAGTAGTAAGTTTAA  
AGAACTTAGTGTAGGCCTGGCATATAAATGATATTGTTGATGTTGATGTT  
AGCTTGAAGGCACATTTATAGGAGTAGGGATTTTATAACATTATGAGCCT  
GAGAGCACATATAATGTTCCC

>Contig11

GGTCTAACATGCTCCAACCTGAAGAAACCCACACTTGTCCGGCAAGGAAA  
CTACTACAGATTTCTGACCTACTGTGCAATTCGGGGCATGCGACGGGAC  
TGTGTTTTCTGGGTACGCTGTCTCAGGTTCTGTCTGGGATGTAAGAATTCAA  
CTTCAGTAGTTCTCTCATAGACGCCGACGAGAGGGGCGTCTCTTTCTCT  
GATGAATCTGCCAGATCTTCCACTTCATAGAGTCTAAATCCTCCGATTCTG  
ATCTACTGGAGACCCCCACGTTACAAAAACGTCTAACGTCCGTGACAGCT  
CCCCACATAGGGAAGATCACCTGAGTCTCACTACCTCACATTAGTGCTA  
TCTCCAGCCCCATGCTATCTACGAGATGGTCACGCGAGGTTTAAGGGGTC  
TCCGATTCCGGTGGTCCGATTACGCTAATCGTGGCCCTACGTGAACGATC  
ACTCCTGCTCGTAACATCGATACAGGGTCCGCGCTGACAAATGGTACTACG  
TAGGTTCTCAGGTCAATGCCGCGTCACGAATGAGCCTAACTACCCCATAA  
GTGCACGTACTGTGTTACCTTCTCTGTTCCGGCCAAACCTGCTACTGTATG  
CTGTGCTTGTTT

>Contig12

AGGCTCCATGTGCTCTAGCCTGATTATCTTTTTCAAGTGTTTTATTGCTA  
ATCTATAAGGCCCTTTTCGTAAATGTTCACTCATTTTTCTAATTAGATAT  
TTTTTTTTAATGTTGAGTTTGGAGAGTTCTTTAGATATTTTAGATACAAGT  
CCATTGTCAAATATGTGATTACAAATATTTCTCTCAATCTGTAATTTA  
GTTTTATCCTCTTAACAGGGTCTTTTGGAGAGCAAATAATTTGATTTTC  
ATAAGGTTCAAATATTAATTTTTCTTGTATAGTTCACACTTCTAGTGT  
TAAGTCTAAAAACTGTGCCTTGTCTATAGGTACCAAAGGTTTTCTCCAGTT  
TTTTTTCTAGAAGTTTAGAGTTTTATGTTTTACATTGGAGTCCATGATCC  
ATTGTTAATTAATTTTTGTATATAGGTAGATGTTTAGGTTTAGGGTTTTT  
TTAAAAAAAATTACATATGTTTAATTGCTCCAGTTCCCTTTTCATTGAAA  
AGGGTATCCTTCCCTCATTGAATTGCCTTTGTGAGAAATTAATTGGACAT  
ATTTGTGTGAGTCTATTTCTGGGCTCTTTATCATGTTACTTTTAAAAAAT  
GCATCAGTTCCCTCCACCAATACCTCATTGTCTTGATTATTGCAGTTATAT  
AGTAAGCCTTAGCATTAGGAAAAGTGTTTTTCTGCTTTATTCTTTINTCA  
AAAAATTTTGGATATTCTAGGGCTTTACATATAAATTTTAAATAACT  
TTGTCTATGTCTAACCGAAAGCCTTATGAAGATTTTGATAAGAATTGCAT  
TATGCCATACATTAATTTAAAAAGAACTGATGTCTTTATTCAAGTTGATT

FIG. 3 (3 of 52)

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CTGCTAATCTATGAACAAGCATCTCTC...CAAAGCATTTAGTCTTTCTT.  
AATTTCTGTCAATTAATTTTTTAAAATTTTCATCCTAAAGATTCTGTATAT  
GTTTTGTTGAATTTATGCTTAAGCATTTCACTTCTTGGTAACAATTATA  
AATGATTTTGTGTTTTTTATTCCACTAGTTCATTTTCAGTGTGTAGAAA  
GCAATGAATTTTGTGTGTTGATCTTTGTTCTACATCTTGCAACATTAT  
TGAACCTCATTTATTAGTCTAGGAGGTTTTTTCATTTTTCTTGTAGATAC  
CTTGAGATTTCTATATAGACAGTCATGTTGTCTGCAAACAGGCACAGTT  
TTATTTCTTCTTTTCAATCTATATGCCTTTTTTTTTTTTTTGCCTTAT  
TGCAGTGGCTAGAACTTCTAGCACTATGTCAAATAGCATTGGTGAAAGCA  
GACATCCTTGTTCCTTGTCTTAGAGGAACATTGGTCTTTAATCTTGGAT  
TGGG

>Cont:q13

GC GCCTCTCTTTCTCTTCCAAAATTTCTCTTGCTAGTTATTTGTCCAGG  
GAAATTTGAAAGCTCACTTACTGTGCAAGTCAGCAGGAAACAAC TGGGTC  
TGTGCACAGCACCTAGCAAAGTTCTGCTCTAGGAATTACACTTTGGCCCT  
GAGGTAGATTTCTACAAGAACCTTACCTTCTAAGCAGCACTGGGGTTCAT  
CTTTTCCCACTCTCAGAGCCCATTTTCACTCCTGAGTTCTCCCCACA  
AAGGACATTTTCAACGGTTGAGTTTATTACTCAACAGAAAATGGAATGAAG  
TCCAAGACCTTAAGGAGATAGAAAGGGGACCGTTATGGCATCTTCTCACC  
CAGGACACCTTGCTGCTAGTGTCTAGTGCTGAACAGACCACCTGGCCCTTG  
CTCTGTAGTTTGAAATGCTCGCTGCAACCAGAAAGGCCACCAAGGGGCCAG  
ACCATGCTCTCCTGTCTATCACGCCTTCAAAGCAGAATTTCCCAAACCTT  
GAGTCACAGTGCTAACACACGGGGTGCCATAACATTTTTGTTGATTTTGG  
CATTTTACAAAAATAAAATAAAAAAGTTAAAAATGCATTGCTCTATTCTT  
GGGGCTGGCACACTATTGCCTTTGGCCAAATCCGGTCCCTGACTGTTTTT  
TFAAATTAAGTTTATTGAAACACAACCATGCTCTTGTGTACATATTGTC  
TCTTGGCTGCTTCCAAGCTACAATA

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>Contig14
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GTGTTTCGCTTTTTAAACACTTACCTAAAATTACTCTGTAATCCATGGATCC  
TTAATTTATTTAAAAAACTAATGTTAATGAGTAGCTTTATTTTCCCTCCCA  
TCTAATTTAAGGCCCCACAGAACACCTTCACTTACCTCAATCCTCTCCCAA  
CTTACATGCTTTTAAATGTCATATATGTTAATACCGTATACTTTTAAAACT  
TTCTAAAAATAGCATTATTTTATAGCATGAGTGTTCATTACATTTTGTGCA  
TATATTTAGAATTTTCTTTGTCTCTTCGTTTCTTCTTCTATTTATGACTCC  
CCTCTGGGATCATTTTCTTCTACTTGAAGTACATAGTTTAGAAGTGCAC  
FATTC AATACAGTAGGCCACTAGCCATGTGTAGCTATTGAAGTTTAAACTA  
AGTAAAAATTGAGTAATATTA AAAA ACTCAGTTCCTTCATCTCAGTAGCCAC  
ATTTCAAGTGCTCAGCAGCCACGTGCGACTAATGACTACTGTACATCAA  
CATATAGAACATTTCCATCATGGCAAAGAGCTCTATTGATAGTGTTCATC  
CAGAGTTTCTGTTCCAGGACCAAACCTGAGGGTTGGGCTGCTATTTCTCAT  
GGCCCAATAACAAGATGCAGATGAGCTGGGGAGGAAGAGAGTTTTTATTT  
CTGCNACCATTTACCGGGAGAGGCCCTGGAAATCATCACCAGGCCAACTC  
AAAAATTATTACGTTTTTCCAGAGCTTATATACCTTCTAAGCTATATGTCTA  
CGTGTAAGTGTGCATTCACTGAAGACGTTAGTGATTAAACTTCTTTTAAAT  
CTGTAACCTAAGGTCTGAGTCCGGAAGATCTTCCCTGGAGCCTCAGTAAA  
TTTACTTAATCTAAATGGGTCCAGGTGCTGGGGTAATTACCCTTATCTTG  
TCCCTTGCTAAATCATGGAGGTTTGGGGATTCTTTAGAGCACCATAAA  
CTTGTTTGTGGAGGCCTGGGGGTTTCTTCTGACCCACAATAAACTTGTT  
TAATCCTAAATGGGTCTGTTAAGAAATCCTTCTTTATTTTGTATATTT  
TAAGGCCCAGAAAAGGCCTGGGCAAACTCTTGATGGGCTTTTGTTACAT  
TCCAGCCTTTGTATAAGAACACTGGTTTTTAATATTTAACTTAACCATTT  
AGTCAGTACTGAAACAGTTGTTATAGAGATCTGCATTATAGTGAGACCTGGC  
CTGCCACATTTCTTTTCTGAAGATCTTATGGTAGTGATCACCTTTGTGA  
AAGGAAAAATAATCTTGGGACCTCAAAATCACTAAGCCAAAGAAAAAAGT  
CAAGCTGGGAAGAATCTGACACTTAAATCCAACACTGCTAACTCATTCA  
TCTCACTCATTCACTCATTTTATTTTCTTTTTTCTTTCTTTTTTTTTTTTT  
TTTTTTGAAACGAAGCTTGTCTGTGTCACCCAAAGCTGGAGTGCAGTGGAT  
CTCAGGTCACCTGCAACCTCCACCTCCCGGGTTCAAGCGATTCTCTACCT  
CAGACTCCTGAGTAGCTGGAATTACAGGCACCTGCCACCAAGCCTGGCTA  
ATTTTTATATTTTAGTAGAGACGGGGTTTACCATTGTTTCATCAGGCTGG

**FIG. 3 (4 of 52)**

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TCTCGAACTCCTGACCTCGTGATCCGC...CCCCCTCGGCCTTGTGCT  
GAGGTACTGTCTAAATGCTGGAAGTGAAGTGGCAAGCAAGACATCCCTA  
CCCTTGAGGAACTGTAATCTAGTCGGAAATACAGATGTCAACCAAGTCT  
CACACAAGAAATTTGTACAAAACCCCTAGGA

>Contig15

GGAAAAACCTATCACCGCCTCCTATGGAACCTTAAACAAAAAGAAAAGTA  
ACAAAGGAAATGAATATTTTCAATCTGGAAGAACATTGAAAAAGAACAGGA  
AGAAAGAGAAAGCACAACTCGAACTGTCCACTAGAATTGACAACACTCTGA  
CAGAATGTCTGAACCTCATCGAAGGGTAAAGTGAATAAATAAGCTCCTC  
CAGCTTTGGCCCAAAGTCTTATAATTTTTAAACATATTCCTAAATATAAT  
ATAGGAGAGATAGCCTTCATCTAAGTAGAAATTTAGCTACTCTTGTAAT  
ACAGAGTAATAATAATATGACATGCCATAAACAGTGTCTTTGTGTAT  
CTGTGCTTTTATAAGCACTTAGCTAAGATTATCTCACATAATTATCATAA  
CCACTGTTACTAGCACTTTACAAACAAACTGAGGCACAAAGAAGTT  
GGAAAACTAATCCAAACAAACTGGCTCCAAAGGAACCTTGCTTTCTTTG  
GGTATCAAGTTCTGAAGAGTACACATTTAACATTGAAACTGAGGTGAGAA  
GGCAAGTTTCTATGTAAAGTTGGAGTATTCTGAATACTCTGGGTAGCTAC  
AAATAGTATTTAAATTTTATCTTGGAATCTGCAGATAAGGATAAAATAGA  
TGGTAGGCAAGAGTATGATCCTTAGGAGAAATTTTCTGAGGAAAAA  
TATATTAATAAAAAATGATGGAATAAACTTCTAAGATCCTTGCTAGAGC  
AAAACTCATTGAGTCTTTGGCTGGTAATGTTGAACATCAACAAAAAAA  
GGAAAAGTTTCAAGTCTTACTCCAGGCAACATTTTCAACATCCAG  
TTAAATATTAACATTTCTCTTTGTGGAATTGAAGTCTTTTCT  
TATCCTCTTTTGGTTGTTGTATTATTTAAAAATGAGTACCTTTTATT  
ATTGAAATCATTCAAGTAATGCAGATAAATGATCAGCCCTCTCCCTGTA  
CAACATACATACTTAGGCATCCCAAACCTCTCTGAGGAGTACCACCA  
TTGCCAGTCATTCTGTTTTCATGCATGTCCATACAGTATAGGTATG  
TCGAGAAATGAAGTATTATTTTGTGAGTTGCAATTCTTTATTCA  
TTTTTGTGTACTTTGGTTGCTTTTCTGTGTTTCTAGTACCAATGTT  
ATGCTGACTTAGGCAGATGAGTTGAGTATTTCTTTTGGCCCTATAAAC  
TGAAAATAGTTTGTATGACATGAGAATTATTTTATTTTGAAGGTTT  
ATAAAACCTTGCCATAAAAAATCGTCTGGACCGGTTTCTTGAGGATGCCT  
GTGTTAGAGCC

>Contig16

CGCTTTAACCTGGGCTACCAATGGTTCGTCAAGTTCTAGATTCTCTATTA  
ATACCTTTTCTGTGTCTTTCTCTGGTCTGTTTTAGCCCCGAGTCTCT  
TAGATCTGTCTCTAATATTCCTATTGACTTTACTTCATTTTCTAAGTCT  
TTATCCTTTTGCTTTACTTTCCGAGAGACCTGCTTAACCTTATCTCCAA  
CTCTTTTATTGAATTTCAATTTCTTTTACTATATTTTTTACTTTGAATA  
CACCTCTCTCTTCTCACATTTTCCCCATAGTATTTTGTCTTCAATTGA  
CAGTTCTACTATCTTATTACTCTGGAGATATTAATAAGTTTTAAAT  
TTATTTATTTTTATTTTCAAAACAGTGTCTTACTCTGTCACTCAGCTG  
GAGTGCAGTGGTGTGATCATGGATCACTGCAGCCTTGATCTCTGAGCTCA  
AGCTATCCTCCTGCTTCAGCCTCCCAAGTAGCTGGAACACAGGCATGTG  
TCACCATACCCAGCTAATTTTTTGTGTTTGGAGTGGAGTCTCACTCTGT  
AGCCCGGTCTGGAGTGCAGTGGTGAATCTGGGCTCACAGCAACCTCTGC  
CTCCTGGGTCTGTTCAAGCAATCTCCTGCCTCAGCCTCCTGAGTAGC  
TGGGATTACAGAAACACACTACCATGCCAGCTAATTTTTGTATTTTTGT  
AGAGACAGGGTTTACCATGTTGGCCAGGCTGGTCTTGAACCTCTGACCT  
TGTGATCTGCCACCTTGGCCTCCCAAAGTGCTGGGATTACAGGCGTGAG  
CCACTGCACCCGGCCACTAATTTTTAAATTTGTTAATAAGACGAGGTCTT  
GCTATGTTGCCAGTATGGTCTTGAACCTCTGGGCTTAAGTAATCCTCCT  
GCCTCAGCCTCCCAAAGTGTGGGATTACAGGTGTGAGCCACTGAATCTG  
ACATTTTTTAAAGTTTTCTTCTTTTACCAAGTCTTTTTTCCCCTTTCT  
GCTTTTTTGGGTTGTTTTATTTTGTATCTCTATCTTGCTAGAACTTTCTG  
CAGACGTTTAGTAATACTAGATTTTTGAGAGTGGGCAACTGGAAAGCTGA  
TTGGAACTCTGAATACATGGGTGAGGCTTGTGGCTGTGAGTGTCAATG  
CTTGATGTCTGGCAAGGCCAATGGGTTTGGGACCCCTACTATTAGTATA  
GGCCTGATTCCTGGGAAAGGCTCTTTGATCTCCTGCCTGGAGGATAAA  
GGCCTGGCTACCAGCCTTCTGTGTGAATGTGAGGGAGAAGGGCTGGAGT

FIG. 3 (5 of 52)

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ATTCAACATCATGCTGAA.CCTTTCAA.JATCATCTTGTTTTTAGTAATC  
 TCCTACCTTAACTCTCTGTCTTCTGCTAGTATGGGAAAGATGACCTGAAA  
 ATCTAACCATTTATTTTTCCCCCATTAAATATCATTTTATGATTATTCAGA  
 AGTTAAATAATTGTCTGCTGTCTCCAAAAAGACTGAATCAACTAGCAA  
 CAAATAAGAAATTTTCTCACAGCTCTGCCAGCATTTTAAAAGAATAGCTTT  
 ATTGAGCCCAGGAGGTCAAGGCTGCAGTGAGCTGTGATTACACCACTCTA  
 CCCCAGCCTGGGTGACAGAGCAAAACCTGTCTCAAAAAAGAAATTTAAG  
 GAACAGCTTTTATTGTTGTAAAATAGACATACAATAAACAGAGCACATATT  
 TAAATTGTGCAACTTATACTTTTGATATAACCTGTGAAAACATCACCACA  
 ATCAAGATAGTGAATATATTTATCACCTCCTGATACAGTTTAGCTCTGTG  
 TCCCCACCTAAGTCTCATGTTGAATTGTAATCCCCAATGCTGGGGGAGGG  
 GCTTTGTGGGAGGTGATTGAATTGTGGGGGTGCACTTCCCCCTTGCTGTT  
 CTTGAGATAGTGAATGAGTCTCATGAGCTCCCCCTCACTCACTCTCTTT  
 CCTGCTGCCATGTGAGGATGTGCTTGCCTCTTCTTTGCCCTTCTGCCATG  
 ATGTGTTTCTGAGTCTCCCTAACCATGCCTCCTGTACAGCTTGCAGAA  
 CTGTGAGTCAGTTAAATCTCTTTTCTTCATAAATTACCCAGTCTCAGGTG  
 GCTCTTTATAGCAGTGTGAAAAGGAACATAATACCTCCTAAGTTACCTC  
 AAGCTTGTTTTTAATTCCTTCTCCTCCCTTCTTCATTGCCAAGCAAACA  
 ACCACCTGTTTTCTGTCACTATAGATTAGTTTACATTTTGTGGGTTTTTT  
 TTTTTTTGAGACAAGGTCTGACTCTGTTGCACAGGAGCAGAGCAGCGTA  
 TC

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CGCGTTATAGGAGATGCGAACTTAAGAAATGATGATAAGGAGACTTTATT  
 AAATATAATTTTGAATTATTTTGGCATTACAGAAATCTAATTATTTAAA  
 ATTCTATTTCATAATTTTAAATCACTGTACTTCCAAGCTTAGCTTAGAAT  
 CCTTCTGTGCTGAGGATTAATTTAATTTGTCTTTATAGGCCTTATCTA  
 AAATCCAAGAATAATTGCCAGAATCAACCACCTTCTAAATCTGTAAGTAG  
 AAATTAGTCTTTTTTAAAAATATGCATTATAAGTATGATTAGTAATAAAA  
 ATAATAAAGATGTTAGCAACCTAAAGAACATGTATTTGAAAGGTATTTCT  
 TACAGATATAAAAAACAGTTTGGTTTAAATAAGAGACAATCATTTTTTGAAA  
 AGTATGACATTTTTTGAAAAGTAGTTTAGTTTATTAAACCAAGAAAAGCC  
 TCAAGTGAACTTTAGTCCTCTTGATAGCTAACATTTATTGAATGCTTACT  
 GTGTGCCTGATACTTTTCTGACTTGCATTACCTCACTGAGTCCTCACAAT  
 CTTATGAGGCTACTATTAGTAGCCCCACTTTACAGATGAGCAAACCTAAGT  
 CACAGAAAGGTTAAATAGGTGCTATAGCTATTAAGTGACAAAGCTGAGAG  
 CCTGTGATCTTAACCACTTTGGTATGCTGCCATGAAGTTAAATAGCTCAG  
 TAGTCATTAAAAGAGAACATTTGCATTGAACCTTCCAAGCCACTTAACAA  
 GTATATGCTTCTTAATCAATTTAATTTAGCTACATTAGATAGAATGGTAA  
 AGGATCCTTAACCTTAAAGTTTAAATGGAAGAAATTAGCCCTCTGAAAGAG  
 GCACAGATTATTCATCTGCAATAAAAAATCTCACCTTTAGTTTTTTAAAC  
 ATAGTTTTTATCTGTGTTCTGAAATGTAACATAAAACAGTGCTTCTGAAAG  
 TGAAAAATCTCACTGGTGAGAATTTAATAAGTTTTAATGATTCACCAA  
 ATCACTTCAGTCATATTTTCACTCATATGCATATGCATATATAGACATATA  
 AGTTTTTATCTGTGTTCTGAAATGTAACATAAAATAGTGCTTCTGAAAGTG  
 AAAAATCTCACTGGTGAGAATTTAATAAGTTTTAATGATTCACCAAAT  
 CACTTCAGTCATATTTTCACTCATATGCATATGCATATGTAGACATATATA  
 TGTTGTATGTATACATGACATCATTAGACACTGTGAAGGATAGCAAAATG  
 TATATAAGGCAAAATTTATGAACAAATGGTTTAACTTTGGGAAGCACTGG  
 GTTACACTTTTACTTTATGCAGATTGAACCAGTATAGTATGCAAGTCTTA  
 AGGAAAAATCTACTGGAAGGGCCCTCATTACAGACTTCCAGAGGCTTCT  
 CTGGAAGTTGACAATACTGACTTCAGTACATCAGCTCGTAAATGAGGATG  
 ATACCTACCTTATCTGCTTTACACAGTTGTAAAAGTAAAAAGTGAACCTCA  
 GGAAGGGAATTACAGAATTTAGGAGAACTAAAAGCACGATGTAAATAAT  
 AGTCATCATTACAGTTATATAATGCTTGACAATTTATATAACACTTTTCA  
 TACATGACAACAATAACTAACACCCAGACATGTTTATATACATTACCTCA  
 CTCAGAACAACCATGTGAGGAAGTTGGCCATATGCTTTAATGTCCAAACC  
 AGGACACTTTTGAGAGTAAAAAGCAGTACTCTTTGACCAACAGGCATAAA  
 TCAAAACTATCTTGTGAAAACCGGATATATGGCATCCTTCTAGATAAT  
 AGATACTTTTACTATTATTAATTTTGCTGTGAATCTAAACCTGCTCTAAA  
 AAAGTTAATTTTAAAAAGTAATGAAGTACTGATACATGCTACAACATGGG

FIG. 3 (6 of 52)

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TAAATCTTGAAAACGTTAAGCTAAGTG...AGAAGCCAGACAGAAAAGG...  
ACATATTACATGATTCCATTTTATATGACACATCTAAAATAGGCACATCTA  
TAGACATACAGAGACAGAAAGTAGACTAGCGGTTGCCAAGAAGTGCAGG  
AGCAGAAGATGGGGAGTGACTGCCAATANGAAAACGCATTACGT

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TGAATCGCAATGATATGTGCCACTTTGCACTCTCTGTGACATATATAATT  
ATTTTAAATGCATTCATTTTTCTCAGAGTGCATTTCGTTTGAAAACATA  
GACGGGAAATACTGGTAGTCTTCTGTGTCAGTTAGAAACACCCAAACAAT  
GAAAAATGAAAAGTTGCACAAATAGTCTCTAAAAACAATGAAACTATTG  
CTGAGGAATTGAAGTTTTAAAAAGAAGCACATAAGCAACAACAAGGATAA  
TCCTAGAAAACAGTTCTGCTGACTGGGTGATTTCACTTCTCTTTGCTTC  
CTCATCTGGATTGGCATATTCTAATATCCCTCCAGAACTATTTTCCCT  
GTTTGTACTAACTGTGTATATCATCTGTGTTTGTACATAGACATTAATC  
TGCACCTGTGATCATGGTTTTAGAAATCATCAAGCCTAGGTGAGCACCTT  
TTAGCTTCTGAGCAATGTGAAATACAACCTTATGAGGATCATCAAATAC  
GAATTCATCCTGAATGACGCCCTCAATCAAAGTATAATTGAGGCCAATGA  
TCAGTACCTCAGGCTGCTGCATTACATAATCTGGATGAAGCAGGTACAT  
TAAAATGGCAGCAGACATTTCTGTCTCCTCCCTCCTTCACTTACTTA  
TTTATTTATTTCAATCTTTCTGCTTGCAAAAAACATACCTCTTCAGAGTT  
CTGGGTTGCACAATTCTTCCAGAAATAGCTTGAAACACAGCACCCCCATAA  
AAATCCCAAGCCAGGGCAGAAGGTTCAACTAAATCTGGAAGTTCCACAAG  
AGAGAAGTTTTCTATCTTTGAGAGTAAAGGGTTGTGCACAAAGCTAGCTG  
ATGTACTACCTCTTTGGTTCTTTTCAAGACATTCTTACCCTCAATTTTAAAA  
CTGAGGAAACTGTGACACATATTAAATGATTTACTCAGATTTACCCAGAA  
GCCAATGAAGAACAATCACTCTCTTTAAAAAGTCTGTTGATCAAACCTCA  
CAAGTAACACCAAAACCAGGAAGATCTTTATTATCTCTGATAACATATTTG  
TGAGGCAAAACCTCCAATAAGCTACAAATATGGCTTAAAGGATGAAGTTT  
AGTGTCCAAAAACTTTTATCACACACATCCAATTTTCATGGCGGACATGT  
TTTAGTTTTCAACAGTATACATATTTTCAAAGGTCCAGAGAGGCAATTTTG  
CAATAAACAAGCAAGACTTTTCTGATTGGATGCACCTCAGCTAACATGC  
TTTCAACTCTACATTTACAAATTATTTTGTGTTCTATTTTTCTACTTAAT  
ATTATTTCTGCAATTTTCCCAATATTGACATCGTGTATGTATTTGCCATT  
TTTAATATCACTAGACAATTCAATCAGGTTGCTACGTTGGTCCCTTGGGT  
TTACTCTAAATAGCTTGATTGCAAAATATCTTTGTATATATTATTGTTTTT  
TCTCCTATCTTGTAATTTCTTTGAGCACATCCCAAAGAGGAATGCCTAGA  
TCAATGGGCACAAATAATTTGACAGCTCTTATTAAACATTATTCTGTAAG  
TAAAAACTGAACTACTTTTCAGTATCACTAGCAACATATGAGTGTATCAG  
CTTCCTAAACCCCTCCATGTTAGGTCAATTATGAACCTATGATCTAACAAA  
TTACAGGGTCTTATCCCACTAATGAAATTATAAGAGATTCAACACTTATT  
CAGCCCCGAGGATTCATTCAACGTAGAAAATTCTAAGAACATTAACCAA  
GTATTTACCTGCCTAGTGAGTGTGGAAGACATTGTGAAGGACACAAAGAT  
GTATAGAATTCCATTCTGACTTCCAGGTATTTACACCATAGGTGGGGAC  
CTAACTAC  
CATGCACACACAATCTACATCAACACTTGATTTTATACAAATACAATGAA  
TTTACTTTCTTTTGGTTCTTCTCTTACCAGTGAAATTTGACATGGGTG  
CTTATAAGTCATCAAAGGATGATGCTAAAATTACCGTGATTCTAAGAATC  
TCAAAAACCTCAATTGTTTGTGACTGCGCAAGAAGAAAACCCCATGCTG  
CTGAAAAGTCAGTTGTCTTTGTCTCCAACCTTACTTCTTTACCTCTCAT  
ATGTTTGTGAATAAGCCCAATAAGCAGACNCCTCCTACAAAGTGAACCTG  
GTCTCTTCTCCTCAACAGG

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GTCTTGTAACACAGGTAAGACGAGTTCAAGTTTTATTTCTTGNTTTTAGA  
ACGGTAGTGAGCGGTTTTTCAAGCTGAGACCACACCTAAGGTAAGTAGCTG  
AATTGGGGTTTTGTCTTGGCTAAAGTTTAAACAACAGCTGGTCTTAATTT  
CTCCTTACCATTAGAGCACTCAGTAATCATATAAGTTGTGTGATCATTCA  
TTTGTCTTAACTGTTTGTCTTCTGTTTTTATTGCTGTTTCAGTCTTTTCC  
CATTGGGTTTGACCTACTCTATCTGACTTGATCAAATCCAAAGGAAATTT  
CCAAATTATGGGAATGAGGCCTCTGAAGTGGCTAAATTTCCACCCCTCCC  
ACACACACAAACGTGGTATGGTGGGGGAAAAACGCCAGCAAAAGAAAA  
AAAAAAGGAAAGATGTTTCAATTTTGACCACCAAACGGGCTTTATTTAC

FIG. 3 (7 of 52)

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ATAACAAGGCCACCTTT...GCTAGCCA...CCATACTGAAAGAGCAATGL...  
TGTTGCCCCATGCTGTGGGTTCCATAGCTAACGTTCTGCCTTTTTTCTTA  
CCACGACAGCCTGGGTTTGGTTCCATAATCAAGCCTTTTCTGGTTTGATA  
CTTGGTAATGCTGAAATAGCAGCAATTTGTCTAGCTGAAATATCGTAAT  
AAGATTTTAAAGATTATTTTAAAGGACCTCAATAGTTAAAGTCAGCT  
TAATTTAAAGCTAACATCCAAGATGTGTGCATGTGTATGTATGCGTCTTT  
GTATTTAAATAGCCCTCATGTTTTTTTTTTTTCTTTCTAGGAACTTGCCTT  
TTTTTGAGCAAAAGTTTTTTTCTTCTCTGTTGACTGGATTCTGTTTTCTT  
CATTACTTCTGCTGTCTCTCTTTCTCTTGCACCGTCTGCTGCATGAGA  
GCCCTAAATAGTTTATAATAGCCTGGGGTTCTTAAAGAAAATGGAGAA  
GGTGCCAGGCTCCCTTTTAGGGAGAACTTCTATTTTTCTTATGGAATC  
CTTAGAGTGTAAACAGACAAGTTTATTTTCTTAACTGCTTGCCTT  
TGTGTTGTGTTACCTGATTTTTTTGACTATTATATTTTTGACTAGCTATT  
GCAACAGAAGCTACTCTTGGGTTTTCAAGGAAGATTGTAGTTTAGACATG  
TAGAAATGTCTTTTAAAAAAAACAACTTTTTTTAAGTGCACTGTAA  
AAGCATCATATGGTCTAGCCTCCTAATAATTTTCTTTTGGAGACCAG  
GATTACAGGGTGGGCTCTGCCCAGAGCTCAGAGATCCAGTTAAAGAGAGG  
TAGTCTCGGCCGGGCGTAGAGGCCAGCCTGTAATCCCAGCACTTTGGGA  
GGCCGAGGCGGGCGGATCACGAGGTCAGGAGATCGAGACCATCCTGGCCA  
ACATGGTGAAACCCCGTCTCTACTAAAAATACAAAATTAGCTGGGTGTG  
GTGGCAGGTGCCTGATGCTCCAGCCACTCGGGAGACTGAGGAAAGAGGAG  
AATCGTTTGAACCCGGGAGGCGGAGCTTGCAGTGAGACGAGATGGCGCCA  
CTGCACTCCAGCCTGGCGACAGTGAGACTCCGTCTCAAAAAAAAAAAGAT  
AGGTAGACTCGATGTTGTCTGACCCGAGCAAGTTAGAGCAACGCCACACT  
TTGAGACGAATTTAAGAGTCTTTTATCAGCCGGCGACCAAGAGACGGCTA  
ACGCTCGAAATCTCTCGGCCCTTGGAAAGGGGCTTGATTTTCTTTATG  
CTTTGGTTTAGGAAGGGGAGGGGAGCTCAGTTGCAACAATCTACAGGAG  
TAAAAACATGCAAGAAATTA AAAAGACAAGTGGTTACAGGAAAACAAAC  
AGTTCCAGGTGCAGGGGCTCTAAATCTATCATAAGATGTTAGGTATGGGG  
GCTCTGCCGACACAACTCAAGGCTTTATGCTGTTATCTCTTGAGCGAA  
ATCCTGGGAACCTCGTACATTGCTTGCTTCAGTACCTTATCAGTTAATCG  
GACTCTTTGATATGTTGGGAGTCAGCGTACACAAGTTAACTCCTTGAGGA  
AGGGGGTGGGTAAGGAGTCTTGATGTCTGGTAAATGAAGGAGCGAAATC  
GAGTTCTCTGGCTTTCTCAGCTAAGGGAGAGCTTATTCATGTGGAAACA  
AGGCTAAGTGATTAAGGGAGAAAGGGAGAGTCTGAAACAAGGTTAGGTA  
TTACAATGTCAATAAAATTTGGTCTCCTTATACAGTCTTATGGTAGATTTT  
TTTCCATCTTTAATCTCCCTCTAGCACCACCAGACTTTTTCTCTCTGTAC  
CTTGAGATGTAAATTTTGCTATCTGAATTTTCTGCTAAGAGTTGTTTCT  
TTAATATGCAAATTTAGGGTTATTTAGCTGACAACTGCCAAAGTAGTGAA  
ACAAGTTATCAAGAACTTGAACGTCTAAGGTAGGAAAAAAAAGTCTTT  
ATGAATCTATAAGATGTACTTCTATTGGCATGCCTAATACGTCTATGTAT  
TTACGTGTTGTGTACACAGTTTTTCACTACTGAAAATATATAGAGGAGTT  
CTAATTAATTGACTTAAGACAATAAAAGCGCTTGAATCAAATACCTTATC  
AGGAAAAAGGAAAAGACAAGTCAAATGCTTGTTCAGTCTATATAACTTA  
AGTAAATCTTTAATAAATAAGCTAGCTTTAACATTATTTGAAATGTCTT  
AAGAATTGCCAGCAGGTTCTGGGTTACAGAATAGTGGGGGTGCAGTGGG  
GTGAGGGTGGTGGGGTGGGNGGTNNNACNNNNNCNNCCCCCCCCCCCCC  
CCCCCCCCCCCCCTCCCCCCCCGCCCCGNGCGGGCCGCGCCCCCCCCCGC  
CCCCCGCCCCCCCCCCCCCGCGCCCCCCCCACCCCCCCCCCCCCCCCCCGC  
CCCCCGCCCCCCCCCCCCCGCCCCCCCCACCCCCCGCCCCCCCCCCCCCGC  
CCCCCCCCCCCCCCCCCCCCACCCCCGCCCCCACGCAACCCCCACCCCCGAC  
GCCCCCGCCCCCCCCCCCCCGCAGCCGACGCCCCCCCCCGCCCCCCCCCG  
CCCCGCACCCCGACCCCCCCCCCGCGCCCCGCCCCGCCCCCCCCCCCCCG  
GCCCCCCCCCCCCCGCGCGCGCGCCCCACCCCCCCCCCCCCAGCCCCGACC  
GCGCGCCCCCCCCACCCCCCCCCCAGCCCCCGCCCCCGCCCCGACCC  
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GGCAGTACGCTATAATTCCTCTTACCTTACCTCATCTGTTCTCTGATG  
GATGACTTTTTTTTTTAGTTTTCTAAATTCCTTTTCTTTTGTCTGGAG  
ATGGGTGATTGATGTAGTCTGGGTATTTGTTCCCTCAAATCTCATGTTG  
AAATGTAAATCCCCAGTGTTGGAGGTAGGGCCTGGTGGGAGGTGTTTGGAT

FIG. 3 (8 of 52)

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CATGGGGGCAGATCCC. ATGAATAG. GGTACTGTCTCTCAATAG. 4  
AATGAGTTCTCCTGAGATATGGTTGTTTAAAAGTGTGTGGCACTCCCCCA  
TTGCTCTCTTGTACTGCTTTTCGACATGTGACATCCCTGCTCCCTTCGC  
TCTCTGCCATGATTGAAAGTTTCCTAAGGCTTCGCCAAAAGCTGAGCAGA  
TGTGGGTGCCATGCTTGTACAGCCTGCAGAACTGTGAGCCAAAATAAACT  
TCATTTCCATATAAAATTACCCAGCCTCAGATATTTCTTTATAGCAACATA  
AGAGTGGCTTAATACAGGCTGGGCATGGTGGCTCACGCCTGTAATCCCAG  
CCTGTGGGAGGCTGAGGGGGGTGGAACATGAGGTGAGGAGATTGAGACC  
ACCGGCTAACACGGTGAAACTCCATCTCTACTAAAAATACAAAAAATTAG  
TCGGGCGTGGTGGTGGGCGCCTGTAGTCCCAGCTACTCTGGAGGCTGAGG  
CAGGAGAATGGCATGAACCCGGAAGCGGAGCTTGCACTGAGCCGAGATT  
GCACCACTGCCTCCAGCCTGGGCGACAAGAGTGAAACTCCATTTAAAAA  
GAAAAACAAAATTTCAAACAGAACAAAATGAAAAAATAACCAAGTGAAA  
GGCCCCCTATAAAAAACCCCTCTGGGGCCCATCTCCCAACCCCTCAAGTGA  
AACCACATTTAACAATTTGGTGCATATCTTTCCAAACCTTTTGTGTACA  
CATATAAAAAACATACATGCTTTGATTTGGCTCAGACTGTACATAGTGTT  
TTCCCTCTTGCACTTTTACACTTAATATATCTTTGACATCTTTCTATGTCA  
GTGCATGTTGGCTCGATGATATTCTATCATTAAATACCCCTCCAAAAATG  
GTAAAAATCATTTTAAAAAATCATTACACAAAGTACATATTTACAATTTTA  
AAAGAAAAACAGAAATCCCAAAACACAACGACAAACCTCTAAAAATAATCTC  
TATCTTTCCACCAGCATGGAACAGTTTCTTCTTTTTCACATAAAACGAA  
TTATGTGATTGGAAAGATTAACTCTAATCTACACATTTATATACAGAATG  
TTCTATTTGTTAAGCCTATCTGAAAATAAAAAATTCAGATGATTAATTCA  
CTTACACTTAGAAATTAAGTCAATATACTATGAATACACATTGTGATCAG  
TTATAATATGATGCTTCTTAGTCTAGGGTTTCAATTAAATAACAGTAAAA  
AAAATTGGATAAAATAAGACAGCTAATAACTGAAAAATCCAGAAATTCAAA  
GATTATATTGCCAACTAAAACACTGCCATTTACATTTTTTTTCTACTT  
GGTAGCAAATGCTAATGGAATTCATCTGATTACTTAAAGTCAGTTCAC  
ATCACACATTCAATCAGGATAATACGAACATAATATGCCTACTATAGCGT  
TAGATTAAGACATAAAATTTTTTGGCTTGAAAGTAATGACTGCGTACCAC  
TTGAGACATTTGTCAACCACTTCAGCACATTGTTTACGAGTGAAGTGGATG  
TCCACAAGGAATAAAACGACAGCAATATTTCTATCCATACAGATTTTGC  
AAAGCTTCTCCTCTTGCAAGGTGTCTTAGCTGCTCTTCAGTACTAATCTCT  
TTCTGCAATGAAGTCTGACTTGATTCTGCTTGTGTACTGTCTTTCTGAGC  
CTTCACTGGATCTGCAATCAGAACCTCAAGTGATTTACAGTTGCTCCCAG  
ATGTCTGAATTTTTTCTCCATTATTTTCTTAATGTCTTTGAAACTGAAC  
CCCATTCAATATAGCTTCTTGTACCATAGGATTATGGAAGATGGTATCAAT  
TTTTCTAGTTAGTGATGGCGTTTTTTTTCAGCAGTTCTTACCAGACACTCCT  
TAAGTGAATGGGATAAATGAATATTGTTTATATATTTTCGTGTCTTCTGT  
CTAACAGATATTTACACCCTGGATGCCATTAAACATGTTGTCCCAAGGT  
CTTNCCTGGGCT

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CTTTCTCCCTTTTTTACCCCAATTTTCGTAGGGATTGGTTAAAACCCATG  
TAAAAATCCAAACACCGGCGGGGAACGGGGGTTCAAGCTCGTATCCCCA  
CCACTTTGGGAACCCAAGGTGGCAGGATTGTGGAAGCCAGGCATTTGAG  
CCCACCCCTGGGAAAAAAGAGAACCCCAATTTTTTTTGAACAAAAACC  
CCAACCCCTCCAGGAAGAAATAAGTATGGCTGGGTGGAAGTCACCAAAG  
ATGGCCGACTGGCTGGTCAAGTAACTTTACCTGATGGTTCGTAGAATATT  
TACCTTCACCCAGGTGGGAGAATTGCTTGAGCCAACCCCTCAGTGTGGATT  
CAGGAACCTGATTTAATTGGTATCGTGATTGTGGATTAGATTCTCAGGGA  
TGCATTCACTAAGTAAAAGTGATAATAGCTACTTTTAAAGTAAAATAATGA  
ATGAATCAAACACTCTAAATCCATGGTGCTATGCTAAGCTCTTTCTGTAT  
TTTATCTCATTTGATATTACAAATATTTGATGTGTTAATAGTAATGACTA  
TCTCCATTTTTTACAAGTAAGGAACTGACATTGAGAGATTAAAAGACTAG  
CACAAATCACAAGTAAATGAGATTTGAATCCGGTCTTGATTCCAAACTC  
TACAGTATTCTAAATCAAGGAGACTAAATTATAAGATGGAGAGCCAATT  
TTACTTTATAACAGGGTTAGAATGGCAGAAGAGACCTGACATTACACCT  
CTAGCCAGTGCATCATCTTCTGTAGGCAAATATGCAGGAAATCTATAAT  
AAGAACGTCCTTTGGTGAAGGCCAGGTGCAGGGGCTTACACTTGTAATTC  
CAGCACTTTGGGAGGTCAAGGTGGGAGGGTCTCTTGATGACAGGAGTTTG

FIG. 3 (9 of 52)

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AGAACAGCCTGGGCAACA TAGTGAGACCTGTCTCTACAAACAAAAACA  
ACACAAAACACTTCAAGAAAACTCCTTTGGTATGGATCAGAACAGATG  
AATTATCTATCTGATCCAAATGCTTAATGACATTAAAGCCACAGTCCACTC  
ACTGCCACAATAGAGATATACCTGCCAATGCCACTCAGGTAATCCCATCA  
AAAGTGGTAATGAGGTCTGCAGCATGACTTGTCTTAGTGATCCAGCCT  
GAGACCTTGAGATTGCAGCATTATTCTACATATGCACAAAACATCTGT  
TGAAAAATCTTCTAAATTGATGCAATACATTCTGTATCAAGAATACCTGTC  
TGTAATCTCCATAAACCTCTCCTTTCTGTTTTAAAAAATAGTAACAGCA  
TTTCTCCTTACATGACAAAGAAATGACTTCACCATCTACGAAATAGTGAA  
TAGGAGCTGTGTGGAAGGAAATTAGCTCTACTTCTTGGTGGAGATGAGAA  
GGGAGTGTCTCTCTGAAAAATCAAGGCTCTTGTCTAGTAGGAGCCAAAGT  
CGTTTTTTAGAGTGTGGACAGTTGAGAAGATAAGACAGGGACCATCCACT  
CATGTTTTCTTATTCATAGGCCTCTCTCAATTGGGCAAAGCACTCCAG  
ACCTTTTGGGAAGAGTGACACCAAAGGCAAGCACCTGCTTGGCAGGCCCCCT  
CAGCTTCTACGCAAGTATAAGTGAGTATATAAAATGGGGTACTTGTGCT  
GTTGAGTACCTTATTTCCAAATGAGGCTGCGGGTGTCCCTGTGGCTGTG  
AGAAGGCCCTCTACTGGATAGGTGGAAGTTGTGTCTCATCTTTCTAA  
CCCTGGATTGACTTGCCCAAAAGGAAGCCATTATTAACACTATAATAAAA  
CCATCCTTAATCTGGGACTCTCTTCATGCAGTGGTTCTTAACCAAGTGATA  
AACATGAGAGTTACTTTTGGAGCTTAAAAAAATTAAGATGCTCAAGGTCT  
ACCCAACTGACTGAATCTCCAGAGGTGAGGCCAGGGATGTATACTTTT  
GAGCCAGACCTCAGTTTACCCTGCAGAGCTCATAAGGTTGCATAACACCC  
TTTGTGAGCCACTCTGATGAAAAGAAAAATTTGGTGAGGAATAAGTTTTAG  
AGAAGAAGGAGCAAAGGTGTTCTTGGCCAGTGAGAGCCAATGACAGGGAA  
ATGCAACAATGTATCCACAAGAAAGGTAAATTACCCTATAGAGCATTTT  
AGGATAAATGAACATCTCATGCTAGGGTTGAGAGAGGGTACAAAAAAA  
AAAAAAAAGACCCTCTGGATACACAACGCGATAAATGGAATAAAGAA  
TTTTTCTCTGTAAATTAAAAAAATCCTTTGTTACTGAGGTATAATTTAA  
TCTATTTTATGTATAGTTCAATGAGGTGTTATAGATAATAAATTTTTTT  
GTAAATTATTATATGTCTATATACTCATACATTCATTTTTAAAGTCAGA  
AATGTATATAACCATTAACCTTATAAATCATTCAAGTCATTAGAGATATA  
GATACACGAGCATATTTTATATCCACCACAATAATTATTACCATCTCAAC  
AATTCATCACCCTCAAATTTCAAGCGTAGGGTTTTTAAATGTCAAAG  
GAGTCTACTCAGTGGGAAGAAAGTTAAGGAAAAACCTTTGGGGCTTTGG  
GCTCCTTCCCCCTGGGGTTAAAAAGGCAGGAAATTGGGCTTACCCCCCT  
GAAATTGGGAACGAAATTTTGGGAAGTTTAAAAA

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TCAAGCAGCCTTCTCTCTGGCTTCCCAAATTGTTGGGATTACAGGCAT  
GAGTCAGGATTCTGGCTTAGTTTACATTTCTAGAGTTTGTATAAATG  
GAAACATACAGAATGTATTTTTTTTGGGAGTGGGGAGTGTCTTATTTCT  
TTTCTTTTCCATTTTCCCCCCCCNCCCCCGAGACGGAGTCTCGCTCTG  
TCTGTTGCCAGGCTGGAGTGCAGTGGTGCGATCTCGGCTCACCGCAAGC  
TCCACCTCCCGGGTTCAAGCAATTCTCCTGCCTCAGCCTCCTGAGTAGCT  
GGGATTACAGGCGCCGCCACCACACCTGGCTAATTTTTTTTGTATTTT  
GGTAGAGACGGGGTTTACCATTGTTAGCCAGGATGGTCTCGATCTCCTGA  
CCTCGTGATCTGCCCGCTTCGGCTCCCTAAGTGCTGGGATTACAGGCGT  
GAGCCACCGTGCCCCGCCCAAGTGTCTTATTTCTTAACCAAGCTTTCTATG  
CAATCTTTTTTTTATTTTACCATCTCTGTGATCCCACTCCCAAAGGTACTA  
GATGTCGATTGGTCTTAGGATCAGCTACCATTTGCCCAACTGCTTTCCA  
GCCTTCCAAAAATTTTTTCTTTTTTTCTTAAAGATACTCCTGTGTGAGG  
CTCAGAACTCTGAATTGCTACTGCAAAATATGAACCTCGGTGATGTGAATG  
CCAGGGAATTGCCTGATTGATCAAAGAAATGTATCCCCTTCTCCCTCACT  
CTTGCTGTCTCTCATTTGTTTTCCCATCCTTGTGGATTCTGTAATTTA  
AATATCCCTTTAATGTTATAATATTTAATGGCGTTTGGCGAAAAGTACA  
GAATTAGGTGCAAGAGTGATAGCTGTTATTTTTTTTTTGGCCTCTGAGA  
CTGTTCAATATATGCAAGTTATTTAACAGAAAGTTCTGCAGTGACCTGAGA  
TGTCAGGGGGGTCTGATAGAGTACGTTTGAAGGCAGTTACTGGAAAAAA  
TAATGCCATTTCTGGTTTGTACTTCGGTAAGTTCAAGTACCCCAATATAT  
TGTTTTACATGTGGCATTCAAGTAAAAAGTAGCTTCCCCCTCCTTTCTCT  
TCCTTTTCTCCTTTCTGCTTCTATAAAGCATCTGCTTTGGGAACTTCT

FIG. 3 (10 of 52)

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TAGGAGGAGAGCTTGGCAJCCCGTGGC .ATGGAGAGGTCTTGCAAGA.  
 AAAAGAGATGCTCCCCTCAATGCAGGATGGTGTGGAGGTAAATGGGGAT  
 ACGTCTGGCATCACTCAGGAATGGGCCTTCTGGCAGGGAAAAAAGGGA  
 GGGGAAAGAGGAAGGGAATTNNANATNAATTGCTGAATACGGGGATTCC  
 ATGGCCTGGATCCAGGAAGAGAACTTTGGGAGGTGTGAACCTGGAAGGCA  
 TCANCTGATGAGGAGCAGCCTGAACTCCGGGGAGGACCTGTTTTTGGTGG  
 CCGGAAAAAAATGCCTTCCACACACAGGGAGGCCACCCGGCTGATGGGC  
 TGGGGGTGGACGGACAGCCCTAGGACAGGCTTGGGAAACCAGGCTCAGG  
 TAGGGCCTGCGAGGTTCTCGCTGCGTCTCTTCTCTCTGGTCTTAGAAA  
 ATAGAATCCAAGGCCTCTTGAGAGTGAAGGTGGGTGGGAGGAGGGCAG  
 ATGGGGCTTAGGCCCAGGACACCCGTAGAGCTACTGCCAGCTGTCTCTC  
 AGGGACTCTGCTGAGGTCACTCCAAGGATCATTCTTAGCCTTGCTAGACA  
 GTACTGACAGAGGGAACCGTAGTATCGCACCCACTTCTTCTCTTCAAT  
 GAAAGTTTTAAAGGTCACCATTTCTCTGGCAAAGGAAGTTCCACAAATAT  
 TCCATTTCCGGTCTTAGAAAACAGCAAGGTATCAAGCAATTGCAAACCTCC  
 TGTGCTGGGGAATTCCAAGGAAGTAGGGGCAGAGTTCTGGTGGAGACAA  
 AGTGAATTCGAGTGATTAGTCAGTAGCAGTAGCAGTAGCAGTAGCAGTA  
 GCAGTAGCAGTAGCAGTAGCAGTAGCAGTAGCAGTAGCAGCAGCAGAACC  
 AGAATTTCCCGCACGTGTCTCAGGCTCTCATTTGCCAACTCAGTCTCTA  
 AGTATTTTTATTGGCAGGAAAAATAAATAGCTATGAGTGAAATAATTCA  
 TTAGACCTGAGCCTCCATCAATTTTGTGTTTAAAGGCCTGACTCTCTTTA  
 CCTTCCCTGGGATGGAAGATGCAATGTTCTGATCTCACTGTCAAAAA  
 AGAAGAACCAGTGGGTATATTGTATGCTTGAGTTCCAGCCATTAGTCACA  
 AGACATAGAGATGACTGCCATGTGTGTAGACTTTCTATAGACTGTGTGCT  
 AAACCCGACCTGCCACTTCCAAGGAGTAGATGAGGAATGTCCATGGTTCT  
 GGGGAGCCCTACCCCAATTTGGGGCAGACATTCCAAGCTCATTCTCTGT  
 GGAGGGGGTGTATGGTTAAAGGAACGGCTGGGATTTACTCTCTCTCTAG  
 GGCCAAGAAAAATGACATGCTGCCTCCATGTTAATCATCCTTCCCCCTGT  
 TAATAACTATGGCTTTAAGTCCCCGGTTAGGGCCTTCTTCCAAAATTGGG  
 GAAAAAATTCCCTCCCCCTTAAAAATTTTTTTTTTAAAAAACCTTT  
 TTTTTTGGGGGTGGGAAAAAACCAAAATTTTTTTTCCCCAGGGGTTT  
 TTTAATTTAAATTTCTCCCCAAAAATTTGTTTTTTTTTTCCGCGAAAAA  
 AAGACCCCCCAAAAAAAGTTTTTTGGCGGAAAAAATATTTTTT  
 TTTGTGTTAAGAAATGGAGAAGAAGGGGGTTTTTTTTTCTTCTCCCCC  
 CACCCGCCAAAGGAAAGTTGTTACAGATTGTTTTGTGTCTCCCCCCA  
 T

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ATGTGCCTGCGAAATCATCCTTCCAGAAATATTTGCCCTTTCTTTTGT  
 ATAGAGTGGCACTGCCCTATATGGTGACCACTTGCCACATGTGGCTGTTG  
 AACACTTGAAATTGGCTTGTGAGAATTGCAGTGTAAAGTGTAACACAT  
 ACCAAATTTCAAAGACATGGCACATAATAAAAAATGTAAATATCTCATT  
 AACAATTTTTATATTGACTGTGTAAGTAACATTTTGAATATATTGGATTA  
 AATACATGGATGATGCCCCAACACCCACAGTCCCTTATCAAGTCTCTACT  
 TCACATTTTTGTACTTCTGACTTAGAAATAGCACTGGCGTCTAAGAGCCT  
 ATTAATGTCGTCAATAGGTTCTTGGGAACCACAATTTTAAACAAAAATGAC  
 ATATAAGAAAACGAATAACATTGAACAAAATGACATTATTGAGGACCTG  
 CTGCAATGTTGTTTCACTTAAAGTCAGTGTCCAAGAACTATCAGTGACAT  
 TTAGTGAGGAATTGCTGTCCTTCTGTTTACAGGAACCTGGGCAAGTTAC  
 TTAATTCCTCTAAGCCCGGTTTATATCCCTGCAAAGAGAGAAGGATAATA  
 ATCACCAGTACTTAGTGATGTGTAAGGAGAAAAATAAATAAATATG  
 AAATGGCTGACAGTGTCTTGTGACACAGAAGATGTGTGATCCACAGTAG  
 CTGCTATTGTCTGCCTCACTTCACTAGTAATGGTCCAGGGAGGCCTTTAA  
 TGTGATGGTGCAGTACATTACATGTTGGACATGGGTGAAGGGAAAGAC  
 CAGGCTCATCTAAACACAATAGGATGCTTGTGGTGTGTTTGGAGGGAATC  
 AAGGACTAGTTATCCACAGCTGTAACATGCATGGATCAAAAGAGATAAGG  
 CACACAAAAGACTTTGTGATAGCAAAGCATTACAAAATGCAGAGACCAG  
 CTGTGGGTGGTGGTGAAGTCAAGCCAGCTTCCCTCTGTGCCTGGCTGAGT  
 GGTTCTGGGCAAGTCAGCCATCTGTCTTGATGCCCTTCCCATCTATAG  
 AGAGGGAGCAACTGAGGCCCTTCCAATACTGAAGTCCTTTATTTCTGCT  
 ACTTTAGAAATATCCACATTTTGGTAAATTCAAATGATCCAATGATTCC

ATTTCTTAATGTTCAAAAAGAGCCCCAACATCTAAATGAATCAAAACA  
AATAAAATATTTATTGTGTATGTTTTGATTGCTGAAACTTCTATTTTAGC  
AACACACACACACACACAGAACCCATAAGCCTTCATCTTCTCTGGAT  
AAACGAGCCTTCTGTCTGGCCATTAAAGTCACGATTAAGTAAATGATT  
CCAACCTCGCCTTTTGCAGCAGTTTCTGATGGGTCTTCTGCGTGGCAGTG  
GCCCTCCTGACTTATGATTCTCTGTGTGTCGGCCTGTTACCACTGCAGCT  
TAACTGAGGAAACAAGAACAAGCCTCTGACCCCAAGAGACTGTTGG  
AGGCAAAGGCTTCAGTCCCAAGAACCTCACACGTGGGGAGCCCGAGAGCC  
CAGCCCTGACCTTTTCTCCAGTAATAACATAAGAAACAACAGGCACTGGC  
CTTATTTTGGATACAAAGAGTGGTGCTTTTCTTAAATCTTCTTTAGTC  
AGGGGTACCCCTTCATGGACGCCCAACATCCATGGTTCTGCTTGAGTC  
CCTGCTTCCATATCTCTGCACTTCTCACTTGAAATATCCCTGGAGTACGT  
TAAGCAGCCAGGTTTGGAGTTCTTGCTGTGCAGGCGGGTGTGTGCATGT  
CCTCTCTCTCAACAGGACACAAGCTCCCCAAATCAGACGGTATGCCTCCA  
CGCCCTTCCCAAGCCTCCCCAGCAGCACCAGCATGTGAGGGGAGCTGG  
GGCCAGGCCATGATGGGAAGCACTCTCTGCCTAAAGACTAGGGTGATGC  
GCCCTCAACTGTGGGAATGAGCCCCAGCTCTGGTGTCTGCCTCGGTTTTT  
CCTCCTGGACAATCAACATGAACTCCTCACCCCTCTTATCCACTTTGCAT  
AAACTGAAAATAACAAACCCAGGGTCTTTCTGTCAAGGAAAGGGTTTTT  
TTTTATAAGATTAAACAGAGATGATTCAACACACCCAGGATATAACACAT  
GGGCCATGAGTCAAGGCCAGGCATTGCTCTGGTCAGCCTGTTGTTGGGC  
CCCCCTGGCAGGGCTCTCCCTGAATCTTCCCCCTCTTGACTCCCCATCA  
CCACAGCACGTCCAGCTTTGGGTACAAGGCCAGTAAATGGGAAGGGGT  
CAGATGACATAAAGAGCCCTTTCTGTCCCATTTGAAATATATTTGGATAA  
CAGATGGCATTTCCTGCTGTCTTGGCCAGGGCCAGAGCCTCCACTTG  
CTAGAGGCAGACAGAGGATGGAGAGCCCTTCATTAGTGGGAGGACATCA  
CAGGTGGGCAAGAAACCACAAGCTTGCACTGAGGCCAGCCTTGAAATAG  
CAGCACCTGCCGGCACCTGTGGTCTGGGGACAGGGTCACAGGATGGAGGG  
GCCTCCTAAGCCTTTTATCTCTATGTACTAAGTACAACCCATTTCCAC  
CTCACAGAGCCAGATCAGCCTCTGTGAGGTCTGGTGGCAAAGGATAAT  
TGCCTGCCCCGCTGCCCGGGTGGGTGCTTGTGCTTGCACTTCTGGGA  
GGTTGTGGGTACTCTGCAATAGGTCTCTCTGACCAGCTCACCCCTCCTA  
CTGCAAACTCAAACCACTTCAAAGAAGATCCAGCACC

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CGCGTAGTCTAAAGACTGAGTCTGAAGCTGTCCCTTCTGCTATGGACTT  
CAGATTTTAGCCCACTTGAATTGCTCCATATCCTCCAAGCCATGGCCATC  
CCTTGACTCTCTGGGCTCCCAAGCACTTGCTGCCTTCATCACACAGTTTG  
AGTTAAGGCAGAAAGACTGGTTTCCATGTACACTTTGTGGAAGCTTTCTC  
ATTTCTTTATATAATCTCTGTCTTTGTCTACTGCTTTAAATCTAGAAA  
TTGTTTACAAACACAAAGGTGATCCTTTAAAGCTCAAAGCTGATTGTGT  
CACCAATATATACCACTCTTAATGGCTTCCCATTAACCTTTGAGTAAAGA  
CTTTATGGAGCCTACATAAGGCCATGACTACCTGGCTCTTATTTCTCTCC  
TCATCCTCATCTCACTCACTCTCCACTCCTATACCCCTCACTCCTT  
CCCCCTCCTCTCTGAGCTCCAGACTCCCAATTACCTACTTCCACCTT  
TTTGACCCCAAGGACTTATCTCAGCCTGGAATTTCCCTCTTTGCTCTC  
CACTGAACCTGTCCACTCCAGTCTAAGACATGTGCTTATGTACACGCCC  
TTACCGTGCTTATCTCAGTTTGTAAATTATCTACTCATTTAGAAAAGTGT  
GATGAAGGTCTTCACTGTGAGCTTTCAGGATAGCAGGAATCATAGCTGAT  
TTTACTTACTTAACGGGGTTTCATTCTTTGTAACTTTTTTTTTTTGGAG  
ATGGAGACTCACTCTTGGCCAGGCTGGAGTGCAATGGCATGATCTCGGCT  
CACTGCAACCTCCACCTCCTGGGTTCAAGTGATTCTCCTGCTTCAGCCTC  
CCGAGTAGCTGGGATTACAGATGCCTGTACCACGCCAGCTAATTTTTT  
GTATTTTTTGTAAAGACGGGGTTTCATCATGTTGGCCAGGCTGGTCTCGA  
TCTCCTGACCTCAGGCGATCCACCCACCTCAGCCTCCCAAGTGCTGTGA  
TTACAGGCATGAGCCACGGCACCCAGCCACTCTTTTTTACTTATGGGTG  
AGAAGCCATTAGAGATCATTTCTTTCTTTCTCTCTTCACTAAGGCA  
CCAGGGTCACTAAGTAGTAGGATACTTTGAACTAGAACTCAAGAAATTGA  
GTTTTAATTTTACCTCACACTCTCATATGAATTCTCATGTGACCTCGGG  
CCATACTTCCCTGTACCCTGTTTCTCTTTTATAAAAGTAAGAGTTTAA  
ACTAGATGGTCTCCGACATGCATCCTTCTCTAACATATTCTGGAACCTTC

FIG. 3 (12 of 52)

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AATAAACTAAGATAAAC AGAATAATTAAAACTTAATTTAAAAGAACA  
 GGAAAGGAAGCAGTTACATTAAAGCAAAAGAGACATCTTCATGGTTGAAGA  
 AGTGTATGCCCTGGTGTCTGGATCCCATTTAGGAACTTGGTAACCTTGC  
 AATCTTGGGCAGATTGCTTAATTTCTCTAGACCATGACTTCTCTTCTGT  
 AAGATGTGATAAGAACATCTACCTCACAGGTTTCATGAGAGGATTAATG  
 AGATAATGTATTATAATCCCTTGAACATGGTAGGCTGTTATGTTAAGTCC  
 TTTCTCTCTCTCTGTAGCTATCATGGAATTTAAAAACACATTATAACTA  
 GAGCATGAGTTGCGACTAAAGGCTCAATTGTCTCTGCATGTGTTGGCTCA  
 TGCATGCTTTATTCCTCTGAAGAGCTTTTATACCAAGTGAAAGGAAATAA  
 TTGCATTTCCCTGAAAATTACAGGAAAAAGTTATGTTTTTCTCTTCATT  
 CAAGTGATTCTGTTAGACCCCAACCACATGCAACAATTTTAAAGTTGCTTC  
 CAAATATATTACAAATATTTCTGTCTTCAAGGAACAATGGCAAGACCA  
 TGAATCAGGTTTACATCCGGATTCCACCACTAACCATGTACCCAATTACT  
 TCAGTCACCTTCATTGAGGTTTACATATCACAGAATAAAATCAGATTTT  
 ATCAGAGGAGGTGAAGACAGGGAGAGGAGATATTTCAATCCCTTCTCCGC  
 AACCCCGTTTTTTTTTTTTTTTTTAAACAAGGATCCTAGAGTTACTGAATG  
 ATAGCACGTTTGAGGGGGAAAGACCCCTAAGGATGATCTTTATAAGCCATC  
 ACTTGGTGTGGTGGTGATAAAAACTCGAGTATCTTTATGCAGTGGAAG  
 GAGAAGATTGGAATCGGAATCAGAAGCTTGAGTTCAAGCACTGGTTTCAT  
 CAGTCTTGTGATCTTGGGTTGGTCACTTAACCTCTTCAAGGGTCTCAGC  
 TGTGAAAGAAGATAGTATCAGCTAATTCTTGATGTGCAGTGAGGAGGCA  
 GTGAGATAGTGACAGGTAACTATAAAACAATTGTCAATGAAACGCATCA  
 CAGTGATTCTTTGGACCCACAAGCTCCAATCTTATAAAACATATCCAGTC  
 ACCCACCACATAGATCATCTCACCTTGATATCTGATTTTGTGGATCAT  
 GGGGAAAAACTGCTGATTCCTAGCAAAACCCATGGCATAGGATAAGTGCA  
 CAATAATTTTTTTTCTTAAATGATTTAGATGACAGTGACTCATTAAAGGG  
 TTTCTGAGGCTCTCAGAGTCGAGAGGTGGGTGCCTGAAGCCACCCAA  
 AGTCCCTGTACAGGATGGCTCCCAACGCACACACCACAGGCTGCCAG  
 TATGTTCCACTATCTACCCAGTAGAGCCCTGCCAGTACGTTCCACTGTC  
 CCTTCCCTAGAAGAGGTGACTGTTGTTCAAGTCCCAGAAAAGCGGGCTC  
 CCCAAAACAATGCAAGGACCCACCTCTCTCTGAACCTCACCCACCCTAGT  
 TTTCTTTAAAAATCAATTTACAAGAAGATCATGTGAAGGAAAAGGTTGG  
 GTGATATTCTAACCCAGTTAGCTGTTTCTCAACCAAGTTCTCTTTGAAA  
 AATTCAACAACCACCTTTGGGGAATTATTTACAACAGAGGAGTGAGGATG  
 GGACCAAGGATAGTATGCTATGTTGGTGGAACAGGGTTTTTTTCTG  
 GATTACCAAGAGATGGTATGCATTGCTCCAGAAGCTAAATATCTTCAG  
 GCTTCAATGGTGGCTTCCACTGAAAATGTTATCCCTGTTGAAGCTTTC  
 AAGCCAGTATTTTATAAGAACTATATTTCTTTGGTGAAGTGAAGCATT  
 ATAATGATGACTATACAGGTTCTTGAGTGACTGAAGCCATCATTAGCATT  
 CTCATTATTTTGTGTTAGTTGCATCTCCATAGCAGCTCACATTCACAATG  
 TGCTTTGCAATTGTTCTTAGCAATAGCCCTCAAGATTCTCAGGAGGA  
 GAGGTTAATCCGATTAAACATTTCTGTGAAGCCTAGCGAGATTAATCGC

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AAGAGTTTTAAAAATTAAGTAAGGACGCCGGGAAACAAATCAATCCCAGCA  
 AACATTTTGTGGGATTTATCATTCAAGCAATTTTACAGTTATCCCTGTC  
 AAATACATTAAGTGTCAAAATGGGCATAGGGGGAACAAAATAATAAAC  
 CCAGCCAAAACAGAATAATCCCTGTTTGTTCATGTTGGATAAAAAAGAC  
 ATTACTATTGGTGAAGGAAATTAGATACATCTTCCATTATTTAGTAAAA  
 TTACCATAACTCTAACTTTGTGGCTTTAGGCAGTCTAGTCCACAGGCAG  
 GAAGGAGGTTTGTGTTGGCAAATGACTGTTATCATCTTCTGTTTCAAAGC  
 TAAACCATAAACTAAGTTCCTCCCAAAGTTAATTCAGCATATGCCAGGA  
 ATGAACAAGGACAGCCTGGACGTTAGAAGCAAAATGGAGTCAGGTAGGTC  
 AGATCTTCTTCACTGTCTCAGTGATGGCAGTTTCATAACTTTAAATGATG  
 GCTATCACAGTTTTTCATAAAATATCTAGATAAACAGTTAAAAATAAATAA  
 TTAGGTAAATGTAGTGGGATAAATATTAGTAGACAACTCACCATAATTT  
 AGAATCTAAAGTAAATTAATAATAATATTTTATTATTTGGTATTTTCC  
 AAGAAAAACATATTGTAGGAAACCATTTCTTTTTAAAAAAAAGTGTCTCT  
 TTTAAAAAGGTGAATAATTTTGTCTAATTCAAAGTTTATTGAAAAGTTA  
 TGTATAAAAACAGGTAAAAGGAACAAGGAAATAAGGGAATGTAAAGAAA

FIG. 3 (13 of 52)

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ATTATAGAAATAAAGTGCATTATTTTGGTAAGAAAGCTTAAAGAGAAA  
ATTTTAGGTAAGAAAGAATCTTACCTAAAATTTGTGCTAGAATAAAGTG  
ACTGGCTAAGAAAGGGATGTTCAAAGCTATTTATGACAAACCCACAGCCA  
ATATCATACTGAATGGGCAAAGCTGGAAACATTCCCTTTGAGAACTGGC  
ACAAGACAAGGATGTCTCTCTCACCCTCTATTCAACATAGTATCGGA  
AGTTCTGGCCAGGGCAATCAAGCAAGAGAAAGAAATAAAGGGTATTCAA  
TAGGAAGAGAGGAAGTCAAATTTTCTCCGTTTGCAGATGCATGATTGCAT  
ATTTAGAAAACCCCATCATTTTCAGCCCCAAAACCTCTTAAGCTGATAAGC  
AACTTCAGCAAAGTCTCAGGATACAAAATCAATGTGCAAAAATCACAGGC  
ATTCTTATACACCAATAATAGACTAACAGAGAGCCAAATCATGAGTGAAC  
TCCCATTCACAATTGCTACAAAGAGAATAAAATACCTGGGAATACAACCT  
ACAATGGACATGAAAGACCTTTTCAGGGTGAAGTGCACCACTGCTCAA  
GGAAATAAGAGAGGAAACAAGCAAATGGAAAAACATTCCATGCTTATGGA  
TAGGAAGAATCAATATCGTGAAAAATGGCCATACTGCCCAAGTAATTTATA  
GATTCAATGCTATCCCCATCAAGCTACCATTGACTTTCTTCACAGAATTA  
GAAAAAATAATAGCCAAGACAATCTTAAGCAAAAAGAACAAAGCTGGAG  
GCATTGTGCTACCTGACTTCAAACCTATACTACAAGGCTGCAGTAACCAA  
ACAGCATGGTACTGGTACCAAAACAGATATATAGACCAAAAGAACAGAAC  
AGAGGCTCAGATATAACACCACACATCTACAACCATCTGATCTTTGACA  
AACCTAACAAAAATAAGCAATGGGGAAAAATAATTCCTATTTAATAAATG  
ATGTTGGGAAAACTGGTTAGCCATATGCTGAAAACTGAACTGGACCCCT  
TCCTTACAACCTTATACAAAAATCACTCAAGATGGATTAAAGATTTAAAC  
ATGGCTGGGCATGGTGGCTCACGCTGTAATCCAGCACTTTGGGAGGCC  
GAGATGGGTGGATCATGAGGTGAGAGATGGAGACCATCCTGACTAACAC  
AGTGAAACCTGTCTCTACTAAAAAATACAAAAATTAGCTGGGCATGGT  
GGTGGGCGCTGTAGTCCCAGCTACTTGGGAGGCTGAGGCAGGAGAATGG  
TGTGAAACCAGGAGGTGGAGCTTGCAGGGAGTGGAGATCACGCCACTGCA  
CTCCAGCTGGGCAACAGAGTAAGACTCCATCTCAAAAAAAAAAAAAA  
AAAAAAGAAAGGATTTAAACATAAGACCTAAACCATAAAAAACCATAGAA  
GAAACCTAGGCAATACCATTGAGGACATAGGCATGAGCAAAGACTTCAT  
GATTAGAACACCAAAAGCAATTGCAACAAAAGCCAATTGACAAATGGGAT  
CTAATTAACTGAAGAGCTTCTGCACAGCAAAAGAACTATTGTGAGAGT  
GAACAGGCAACCTACAGAATAGGAGAAAAATTTTTCAATCTATCCATCTG  
ACAAAGGGCTAATATCCAGAATCTACAAGGAATTTAAACAAATTTGCAAG  
AAAAAAAAACCCATCAAAGTGGGCAAAAGATATGAACAGACACATCTC  
AGAAGAAGACATTTATGTGGCCAAACATGAAAAAAGCTCATCATCA  
CTGGTCATTAGAGAAATGCAATTTGAAACCACAATGAGATACCATCTCAT  
GCCAGTTAGAATGGCGATTATTAAGAAAGTCAAGAAACAACAGATGCTGGA  
GAGGATGTGGAGAAATAGGAATGCTTTTACACTGTTGGTGGGAGTGTGAG  
TTAGTTCAACCATTTGTGGAAGACAGTGTGGCAATTCCTCAAGGATCTGGA  
ACCAGAAATACCATTGACCCAGCAATCCATTACTGGGTATATACCTAA  
AGGATTAGAAATCATTCTATTGTAAAGACACATGCACATGTATGTTTATT  
GCAGCACTATTCACAATAGCAAAGACTTGGGAACAACCTAATGCCCCACC  
AATGATAGACTGTGTAAAAAATGTGGACGTATACCCCATGGAATACTAT  
GCAGCCATAAAAAAGAATGAGTTTATTCTTTTGCACGGAACCTGGATGAAG  
CTGGAAGCCATCATTTCTCAGCAAACCTAACACAGGAACAGAAAAACCAACA  
CTGCATGTTCTCACTCATAAGTGGGAGTTGAACAATGAGAACACATGGAC  
ACAGGGAGGGGAATGTACACACCAGGGCTGTGAGGAGGTGGGGGGCAA  
GGGGAGGGATAACATTAGGAAAAATACCTAATATAGATGACGGGTAAATG  
GGTGCAGCAAACCACCATGGCACATGTACACCTACGTAATAAACCTCCAT  
GTTCTTCACATGTATCCCAGAACGTAAAGTAAATTTAAAAAAGAAAGAA  
AGAAAGAAAGGATGTTACGACAAACCAGAAAGTCCAAGCATGTGATGA  
ATAGTCTGTGTAAGTCAATAAGAGGATTTATTTAAAAAACTTTTATA  
TGATAAAGTTGTCTATAATTAAAGGGAAATTTAATGGTCTTTCTAGAGA  
TTGGGTTGATGTTAAAAAACTACTTATATATTAAAAAATTGGTTAGAACA  
ATGAAATTTTCTTACGGGGTTGATTCACTCTTAATAAATTATAAGAGACT  
TAAGAATTTTTTTTAAACCCAAAGTTTCAAGCTTTTATTGCATCTTGTGTT  
TTAGGTTTTCTCTCCCTTTTAAAGGGTGGGAAATAGTAATGCCCTCCTT  
CAACTCCCTTCAGCTCATATACGTTTTTTTACCCTCAGATTCTGTTTGTG  
TGCTCTGATGCTAACAATGTTTTCTTAAAGGTCTAAAGGAAATGTTTTCT

FIG. 3 (14 of 52)

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TCCAACATAATATTCTGTGCATTGCGAGAAGGTCTTTCTTTTGCCTTTTG  
GTAAGTGGCTTAACAGATTTTATGTTTTATTGAAATAATTTCTATGCCAT  
TATTATTAAGTTTTGGTTTGGCTTAGAAAACACTGAGATTAATACAATTTT  
TAAAAATTATGATTATTACATCCATATATCTTTATGTATGTGCTTTTAA  
AGTCCTTGTGACATTGAGTTCTAGGGCTTGACTCCTGGGTCTTAAAAGGA  
CAAGTCCTGCTAAATCTTAAATACTGACAGCAATTAAAGGCTCATCTTCA  
GGCTGGTAGAAAATGCCAATCAAAATAAAGTGCATTCTTGAAACACAGA  
GCCAGAAATTAAAGCTATTCAACTCAAGGCCAGGAAGTATAGTGGAAGA  
GGTGGGTGTGTGAGATTGTAAGGGCCAATTTTGAGAGATAAAATAAGTTC  
AATTTCTCTATAAATTAATCATAATCATTGATGTCCAAGCCACACTGATG  
CAAGATCAGCATATGGGTCTGTGTGAGATTAAAGGTTTTCTTGAAGC  
ATTAACCTACTCCTTAATAAAGGTTATAGAGGTTATAAAGGCTTCTGGA  
AGTTATAGTATGGTCAAGATAAAAATTTATAGATTGTTAATACAATTT  
TGGAAAACAAATTTAATTGGCTTCTTGCTGTTTTTATTAGGGCTTATTGT  
TTGAAAATTAAGTCTCGTCTCTCAAAGAAATGAAGGCTTTCACCTTTTTT  
TTTTTTTTTTTAAATCCTTGAGTTATCACTTTGGTCAAATGAATGACTTA  
TTTTACAATGACCTTTTATCAAGTGTTTTAAACCTTTCAAATTTGACAAA  
CTTTCCAAAATCAAATCAAAATTAATGTCTTTTATGACCTAATGAATCC  
TTTAAATACTAGGTTCCCTAAAGTCCAAAAAATAACATAA  
TGTGGCTTATTTGGTATAAAAAATTTACAAGAAACATTGTCAAATATAAA  
ATATTGTGTGGTTTTGTTTGGGCTGTATTTGTATAAATATGTTATTGGTA  
TGTGTTCCAAATTAATAGGAACTCCTATAATTCTGATATGACTTGGTGT  
ACATTATCAGTAATAATTATAATTGTTATGGTAAATTAATTGTGTGCCATG  
GAGGTAACAAATTTCTCATCAAGTGTGTCTTTGACTATGGTTGCCCTAA  
AACTTTTGGCATTACAGACAATTGTCTTGGTCTTTGGTCTCTTTAGAAG  
GTGGTTTTATAATCAGCTATAAACTCTAACGGGTGCTCTTGAATGCAGG  
CTTAAGATAGCTTTGGAGACTGTGACATCAGAAATAGAGGAAAACTTTCA  
GTATTCTAGGAGTGTGAAATATTATGAATATCAAGCAAAACAGGAATT  
AACTTCATAGATGGAAGTAAAGAAATGCTGAAGTAATCTTTTTGACTTTT  
TTTCTTAGAATGTTGATCTTCTGTTTTGTTTTTCTAGAGTCNAGGAAATTT  
TTCTGTTGAGATATTGACAGCTTTAACAATTAAGTATACTCCAGTGAACA  
CAATTTGGAGCA

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ATCTAGTCATTCCCCAGCCTGACCAATTCAATGGCCCCCATCTTAGTTAA  
AATTCCTCACCCTGACAAGGCCCATCTACGCCCTGACCTCATGCCCTC  
CACTCTCAGATTTGCACTCACCCTGCCCACTCAAGGGCTTCCCCAGGTT  
CCTTCTTAGATTCCACCGATAGCTCAGGGACTTTGCACATGCTACGGTCT  
CTGCCCTGGCTCCTCCCAGATCTTCTCATGCCCTAGCTGCTTCTCATCAGC  
ACCCCTCAGAGACTGTCCCTGCCCCACCTCTCCAGGTTCCATACCTGCCA  
CCCTCCCCCAATCAGTAACAGTTTCTTACAGAGCGAGTTACCATCCCA  
GTATTTCCCTAACTTATTTTTGTGACTGGTCTGTGCCCTGTCTCCACCA  
CAAGAACATAAGCTGCATGTGAACAGGAGCCTTGTCTATCTTGTACCCCC  
AGTGGCTGTGACATAACCTGATACACATTAGATGCTCAATGATGTTTGAT  
GAATGAAGTGTGGTAGTCCAACTGTGTTTCTTGTCTGTGTAAGTATGT  
CTGTTGTGGTTTCTTAAGAACCTACAGCTCTCCACTGTGACTCCTGTTT  
TATGGTCTGATTTGCTGGACTAGAATCCTAACCTACATGCTTACTCTTA  
GTGTCTCTCCCCAGAGGCTGAATCCAGTCCCTAAACCTCCACCAAATGG  
CTAAGACCTAGCTTCCAACCAGACAGGCTACGCTGAGACCTCAGCACCG  
CCCTTCTGCGGTCTCATCTTAACGCATCCTTCAGGGCCCAGCTTAAATG  
TCTCTTCTCAAGGAAGGCTATCCTCTTTCTGCCCTCAGTGTCTCTCAT  
GCCTCCTCTATGCCTCCATGCCTGCTTTCAACCCTGCAGAAAGTGGAGAAA  
TTGCTAATCTGCTGTGTTGACACTGTGCTGGGGTGCTTTGGGCCAGGGAG  
CAGGCTGGTGGTGTGCTGATAGCCCGTGGCTGTGCCCAGGTCCATGCTCA  
CTTCTGAGCCCCAGTGGAGTAGGCTCCCTTTCCCTTATTGCAGCACTCA  
GAGGAAGGACGTGCTTCTTAGGACAGATCTGGCCAACCTCTCCCTCGTGA  
GAGAAGGCCAGCCATCCTCTTGCCCTCTTTCTTCTCTGCCCCGAGT  
AATAAAGGTGCCTGGTCAAGAGCCTTCTAGAAGGAGACCCAAACATCCACC  
ACACATTCCCAGTTCCAACCGTCATCCACATGGCTGGCTGTGCAGGTAAA  
CGCAGAGTCTGTTTCAACACACCCCAACCATCTAGTATTGGATGGGAGGACA  
GTAGCGTGACACTCTTCTCCAGCCTTGAGCCCTACTGTGGGGCCCCACCCA

FIG. 3 (15 of 52)

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ACCCAGATACCAGAGGAGCCCTGTACTGGGATGCTATTGGATGCTTGAC  
AGTCATGTACAAAGTTAGCCCTTTGTTATATAGAGTTAGCTACGTACATC  
TTCCTCTGTAGGGAACCCAGAGGGGAGAGATATGTAGTAGGATTTA  
ACCTGCAAATCCTCTGCTGAGCACCTGCACTACATACAGTGGGTAGCAT  
GTGGTAGGTGCTCAATAACTATTGACCGATAGATTGAATACAGGTAGGAT  
GGTGACACAATCTAAGATCCAGGGGTGGGGAGACCACACGCTTGGTTAG  
GGAGACCCAAAGTGGACCGTGTGGCCAGAAGAGTCCCGCACTGCACTCTA  
GTGACAGTGCAGAAAGTCACTGTGGGAAATCTAGAAGTTTCTACAGGTTG  
CTATTTTCATCATAGCACTGTGCGAGGCCAACCCCTTCTGCTCCACTGGCTG  
TTGGGAAAAGCTTTCTCTTTTCTTCTCTAGCCAGGGAGCTCTCAAAGTGT  
CCACTCTCTCACCTCCACCCAGGCGTCCAGGTGTGGAGGACACTTGCCGG  
CTGCTTGTCTGCTGACTCATCCCTTGGTTTCACTTGGAAAACCTACCACC  
AGCTGGCCCTCTTCCAAAGCATCAGCCTCCTCATTTTCTTAATCCCTTAGG  
TGTGATCTCACCTCCACACAGTAGATTGCCTCAAGGCCAATTCCAATAT  
GAATAAAAAATGATTATTTTGTCTCTTCCAATCTTCTTTTAAAAATATTA  
TTTTATAATTTCCCTTTTAGGAGGATCACCTAAGTGAAGACTATTTTACCT  
AAGAAAATGTTAAAGTGTAAAGACATGGTTGTAATCTGGGGATTCTGTTA  
AAATGGCTAGCAGACAGAAGTCAGACGACAGGCTAGAAATGTGTGAAGAG  
TGGTTGCCCTTTGAAAGGCGGAGTTGGTAATGATTTTCTTCCATTTTCCA  
TGCTTTCCAATTCTCTACAAAGGCCCTTAATATTACTTCGATAACCAGGAC  
CTCTGATAACCTGCCCCCAGGAGTAAAGACTTAGCTGGGAAAGTCAGCT  
TCATGTGAGGTAAAGGAACCAGGTAATACACAATTCCCCTGCAACTG  
TCGGGTGTGAGGCTGAGCTTCTGCTGTGGGAGGAAAGAGAAAGAAG  
AGAGAACTCCAAGATCCAAGAGATCCAGCAAGAAGGCTGGAGTCTGAGG  
ACGCAGAAAGCTGAATGGCACAGTTACCACTATTGTGCTGAGGTTCTGTG  
GCCTCTGGGTCTCTTGACAACCTGGGCAAAGACCCACAGAAAATCTCTCT  
AGACCCTACCTGTGGGAGGGGAAAGTGCTTAAGATCTTTACAGGACAGC  
CACCTGGACCTCAAATGGCTTACAGTTCTTTCATCCAGAGGGTCTTCATT  
TAGTACATACCAGGTGCTAAGCTGGGTGCTGGAGACATGACGGGGAACCC  
ATTTACCATGGCTTTGTTACTGTGACATTACATCTAGGGAAGGCCAGCA  
AAGGGGAGGGATCGAGGAGAGCTTGTAGGCAGAGAAAATACCCAAGGGC  
AAGGGAGAAGCCAGCCTGTTCTGAGCACACACAGTGGTTCCATCTAACTG  
GGCCTCAGTGCCAGGTTGGACTGGAGATGGGGCTGAGGAGCTGTACAGA  
GCATTCTGGACACAGATGTACATAGTCCCTTGAGGTTAGGGTCTTAGG  
CATGGCAGCATTGCTTTGAGTTTTTCTTTTGTAAATGTTGCCATTCTGA  
CAATGTGGAAGATGGGTCTTGAGAGAAAGGGCAGGGCTGTGAGACCAGT  
TAGGAGACTAAGATGTGAGCCAAGGAAAATGAGGAACACCTGAACACTGG  
GGCAGGTGACGGGCCAGAGAGAAGCAGATGGCTTCTGAGGTTTTAAGT  
AGGTAGAATCAAGGCAGCTGGTACAGATCTTTTATTACATATAAACTGGA  
ATAAGCCATCTGTTCCAAGACAAAAGAGTAGGCGGAAAACAATACAAGAC  
AGAAATGGAATTAGAACAAACCTGGGAGGAATGTGGAATTAGAGTAGAGA  
GTCCAACACTGGCTGCAATCATAAAAAATGTAAACAAACAAAAATTTGCT  
AGGTGTGCTTACTTAGAAATAATTAGCTGTCTATTAAGTTCACTTGTGT  
TATGGCTTAAATGTGTCCCCCAAATGTGATGTGTTGGAACTTGATCCC  
CAATGCAACAGAGTTGAGAGATGGGACCTTTAAAAGGTGATTAGGTCATA  
AGGGTTCTGCCCTCATAAATGAATTAATACTGTTATCATGAGAGTAGATT  
CCTGATAAAAGGATGATCTCTGCCTCCTCCCCACAGCCCTCTGTGCTG  
CTTTCCTGCCTTTCCACCTTCTGCTATGGGATGACACAGCAAGAAGGCCC  
TCACCAAATGCAGCTCCTTGATCTTGGACTTTCAGCCTCCAAAACCTGTA  
AGCCAAACAAATTTCTGTTTATTATAAATTACCCAGTCTCAGGTATTCTG  
TTCTAGAAACACAAATGGACTAAGATCATTAAATTATCATTTTTTATCA  
GACTGTTGA

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AAAATATAACAGAGAGTAAGAGGAAAATTACCTTCTTTCTTTTCTTTTCT  
CCTGCCTGACCTTATTCACCTCCCATCCAGAGCATCCATTTATTCCATT  
GATCTTTACTGACATCTATTATCTGACCTACACAATACTAGACATTAGGA  
CAATGTGGCCTGCCTCCAAGAACTCAAATAAGCCAACCTGAGATCAGAGA  
GGATTAATCACCTGCCAATGGGCACAAAGCAACAAGCTGGGAGCCAAGTC  
CCAAAATGGGGCCTGCTGCTTCCAGTTCCTCTCTGCTGCTGCTGCTGCTG  
GCATTATCCTTCTGCTCCAGTCTGCTCTCCACTACCACTTTCCCCCTCAA

FIG. 3 (16 of 52)

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CACACACACACACAACAGCTTAGATGTTTTCTCCACTGATAAGTAGGTG  
 ACTCAATTTGTAAGTATATAATCCAAGACCTTCTATTCCCAAGTAGAATT  
 TATGTGCCTGCCTGTGCTTTTCTACCTGGATCAAGTGATGTCTACAGAGT  
 AGGGCAGTAGCTTCATTGATGAACCTATTCAACAAGCATTATTCACTGAG  
 AGCCTTGTATTTTTCAGGCATAGTGCCAACAGCAGTGTGGACAGTGGTGC  
 ATCAAAGCCTCTAGTCTCATAGAACCTTAGTCTTCTGGAGGATATGGAAAA  
 CAGACAACCCAAACAACCAACAAAAGAGCAAGATGCTGCAAAAAAAAAAAAA  
 AAATGAATAGGGGTGCTAAGATAGAGAAAAGTGGGAGAGTGTCTTTTAGAC  
 AAAGTGGTAAAAAACAAGCCCTTGTGAGATGAGAGCTGCCGACAGGAGG  
 GGGCGGGTCTAGGTTGTGGGTTTTTGGGTAGGACATTCAAGAGAGGGGGC  
 GGGTCGTGGTTGTGGGTTTTTGGGTAGGACATTCAAGAGAGGGGGCGGGT  
 CGTGGTTGTGGGTTTTTGGGTAGGACATTCAAGAGAGGGGGCGGGTCTGTG  
 GTTGTGGGTTTTTGGGACATTCAAAAGAGTCTGAATGCACCCAGGCCTAC  
 AACTTCAAGATGGTAAAGGACAGCTCCAAGGATCAGAAGAAGCATGCTTG  
 GAACTGGGGCATTGTGAGAAGGAGGAAAAATATGCAGAGACTAGTGCTTG  
 CAGAGCTTGCATGTGGATTTTCAATTTGAGGTACAATGAAAACCCATTAATG  
 GGTTCACACAGTGCATGGCCTGACCTCACTTATATTTCTAAAATAGA  
 AACAGATCAGAAGGAAGGCAATAGAGAAGCAGAAAGTCCAATGAGGAGG  
 TTTACAGCAGTCTAGGGGTGGGTAAGGAAAAGAAGTGGAAAGAAACA  
 GACAGAATTGGGTTATATTTGGAGATAGAACCAACAGAAGGAAGAGGAG  
 AAACAACATTTACTGAGAAGGGAAAAAGTAGGAGAGGAATAGGTTTGGGA  
 AATAAATCCTGCTGACATTGGAAACCCCAAGGAAGCCTCAAAAGTATATT  
 TACTTGCCTTTAGATTTAAAAGAATAGGAAAGAAGCATCTCAACTTGGAAAT  
 TTGAAATCTATTTTCCATAAAAAGTATTGTTAAATTTCTACTCATACTCAC  
 AAGAAAAGTACATTTCTAAAGAGTATATTGAAAGAGTTTACTGATATACTT  
 AGGAATTTTGTGTGTATGTGTGTGTGTGTATGCGTGTGTGTGTGTTAAC  
 CTTCAATTGTTGACTTAAATACTGAGATAAATGTCTATAATGCTAAAT  
 TGATTTCCCAAAGGTATGATTTGTTCACTTGGAGATCAAAATGTTTAGGG  
 GGCTTAGAATCACTGTAGTGCTCAGATTTGATGCAAAATGTCTTAGGCCT  
 ATGTTGAAGGCAGGACAGAAACAATGTTTCCCTCCTACCTGCCTGGATAC  
 AGTAAGATACTAGTGTCACTGACAATCTTCATAACTAATTTAGATCTCTC  
 TCCAATCAACTAAGGAAATCAACTCTTATTAATAGACTGGGCCACACATC  
 TACTAGGCATGTAATAAATGCTTGCTGAATGAACAAATGAATGAAGAGCC  
 TATAGCATCATGTTACAGCCATAGTCTTAAAGTGCTGTTTCTCATGAAGG  
 CCAAATGCTAAGGGATTGAGCTTCAGTCTTTTTTCTAACATCTTGTTCTC  
 TAACAGAATTTCTCTTTCTTTCTCATAGGAGATGCCTGAGATACCCAAAA  
 CCATCACAGGTAGTGAGACCAACCTCCTCTTCTTCTGGGAAACTCACGGC  
 ACTAAGAACTATTTCACATCAGTTGCCCATCCAACTTGTTTTATTGCCAC  
 AAAGCAAGACTACTGGGTGTGCTTGGCAGGGGGGCCACCCTCTATCACTG  
 ACTTTCAAGATACTGGAAAACAGGCGTAGGTCTGGAGTCTCACTTGTCTC  
 ACTTGTGCACTGTTGACAGTTTATATGTACCATGTACATGAAGAAGCTAA  
 ATCCTTTACTGTTAGTCAATTTGCTGAGCATGTANTGAGCCTTGTAATTCT  
 AAATGAATGTTTACACTCTTTGTAAGAGTGGAACCAACTAACATATAA  
 TGTGTTATTTAAAGAACCCCTATATTTTGCATAGTACCAATCATTTTA  
 ATTATTATTCTTCATAACAATTTTAGGAGGACCAGAGCTACTGACTATGG  
 CTACCAAAAAGACTCTACCCATATTACAGATGGGCAAATTAAGGCATAAG  
 AAACTAAGAAATATGCACAATAGCAGTTGAAACAAGAAGCCACAGACCT  
 AGGATTTTATGATTTTCAATTTCAACTGTTTGCCTTCTACTTTTAAGTTGCT  
 GATGAACCTCTTAATCAAATAGCATAAGTTTCTGGGACCTCAGTTTTATCA  
 TTTTCAAATGGAGGGAATAATACCTAAGCCTTCTGCCGCAACAGTTTT  
 TTATGCTAATCAGGGAGGTCAATTTGGTAAAATACTTCTTGAAGCCGAGC  
 CTCAAGATGAAGGCAAAGCACGAAATGTTATTTTTTAATTATTATTATA  
 TATGTATTTATAAATATATTTAAGATAATTATAATATACTATATTTATGG  
 GAACCCCTTCTCCTCTGAGTGTGACCAGGCATCTCCACAATAGCAGAC  
 AGTGTCTTCTGGGATAAGTAAGTTTGATTTTATTAATACAGGGCATTG  
 GTCCAAGTTGTGCTTATCCCATAGCCAGGAACTCTGCATTCTAGTACTT  
 GGGAGACCTGTAATCATATAATAAATGTACATTAATTACCTTGAGCCAGT  
 AATTGGTCCGATCTTTGACTCTTTTGCCATTAAACTTACCTGGGCATTCT  
 TGTTTCATTCATTCACCTGCAATCAAGTCTTACAGCTAAAATTAGAT  
 GAACCTCAACTTTGACAACCATGAGACCACTGTTATCAAACTTTCTTTTC

FIG. 3 (17 of 52)

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TGGAATGTAATCAATG1. TCTTCTAGGTTCTAAAAATTGTGATCAGACCA  
TAATGTTACATTATTATCAACAATAGTGATTGATAGAGTGTTATCAGTCA  
TAACTAAATAAAGCTTGCAACAAAATTCTCTGACACATAGTTATTCATTG  
CCTTAATCATTATTTTACTGCATGGTAATTAGGGACAAATGGTAAATGTT  
TACATAAAATAATTGTATTTAGTGTTACTTTATAAAATCAAACCAAGATTT  
TATATTTTTCTCCTCTTTGTTAGCTGCCAGTATGCATAAATGGCATT  
AGAATGATAATATTTCCGGGTTCACTTAAAGCTCACATTACACATACACA  
AAACATGTGTTCCCATCTTTATACAACTCACACATACAGAGCTACATTA  
AAAACAATAATAGGCCAGGCACGGTGGCTCAGACCTGTAATCCCAGCAC  
TTTGGGAGGCCAAGGTGGGAAGATCACTTGAGGTGAGGAGTTCAAGACCA  
GCCTAGGCCAATAGTGAGATCTCATCTCTACAAAAAATGAAAAAT  
TAAAAATGAGCTGGACATGGTAGTACACACCTGTAGTCCCAGCTACTCG  
GGAGGCTTGAGGTGAGGAGTCACTTGAGCCTGGGAGATGGAGGCTGCAG  
TGAGCCATAATCACACCATTGCACCCCAACCTGGGCAACAGAGTGAGACC  
CAGTCTCAAAAGATAAATTTTTAAAAATGTTAAAAATATATAAAAGAGA  
ATTTTAAAGAACAATAATAGATCAAAGCATGGATGCAAGATATATTTA  
GTTGGAAAATCAAGGTTAAAAATCAAGGGATCTTGGAAATTAGGTGTGGTAG  
ATTTGGGTAAGGAGTAGTCTAAGATGACCCTGTTTCTTGGTACTGGAGAC  
TGGATGAGTGGCAGCGTCTTAACCATATTTTGGTAGAAATATGGAGGTC  
TTCTCCATTCCAGGATGAATGATGAGTAAAATTTAGGCATGTAATTTGA  
GCTACTAGAAGGCACTCAATTGCAGATGTACAATGGGGAGATGATAACC  
TATCTGGAATCAGAAAAATAACTGTATATAGATATGAAAGACATCAGTA  
GGTATGTAGTAGATAAAATCCTAAAAGTGATGTCAAAGGGAGAAGAGAAG  
TATATGGTGAACACTGTTGTTTGTCCATGCAATTGCCATCTCTTCTTCTT  
CCTTACTGACAGAACCCTGATTTCACTGAGAAGTCAACATGCCCTTCCCC  
AATTGATGAATCCAATTGGTTGAAGATTATGTTCAATCTATTCTTACATG  
ACTAAGTCACGTTGACTTAATCCTATCAAAATGAGATGTCGATCTGGAAAC  
AACTTCTGGAAAAGATTTTCTACCTTGATAAAATAAAGAGCCATATAGAT  
GGTCCTTTATCTTCTTCTTCTTCTTGAATGAGATATGTTCTATGAGGAAGT  
GAAGCTTAGAAGTGTGGTCAGCAACTTGCAACGACTGGGAAGTCAGAGCC  
ACACAATGAAGAATGCAGAGTGGGAAGGAGAAAAAGAGCCAGCATCTCTGA  
CAACATTGTTACACCGAGAACCCTACCTCCAGATTTTAAGAAAACAAGAAA  
TGCTACTGTTATTAAGCCATTTCACTGGGTTTGCTATGACTTGCAGTCAA  
ATCTAGCTTAACTGATACAGAGCACCACAGAGAACTGGTCTCTCATTGT  
CTCATCTGTTCTTTCTAGCAGCCACGACTTTCTAGGGTTTCTTAGCC  
CAAGCTGGCTAGAGCAAGACTAAGTAAGACTTGATTCTTAAATGTCCTT  
TTGTTTTAAGAAATATTAAGAATTATTTTTATATTAATATATTTAAGA  
AATAAGGAAATACAAACACTGAGCAAGCAACACAAATTCAAGAAATCTT  
AAAAAGTATAATAGCTGCTCAGTCTCTGATTAAACAGTGAAATATGGAATC  
ATTGTAGAAATGGCCTTGGAGCGTTATTCTCCAGGCCAGCTATCCTTAT  
GGTCTGCCCCACCTCCCTCATTGCCTAAACAGTAAGAGAGTCCCATGGTG  
AGACTCAACAGTCTTAGCACAGAACTTGTTACAGTCTATTTCTTTCTTA  
CAGTCTTATATATCAATTCCAAATCAATGAGAGTAAAGCCCAATCCCTGC  
CTTTAAACCCAAAGGACAGAAGCCCAAAGCCCAAAGATATTCCTAACCT  
TCTCCCCCT  
>Contig28  
CCTGTGCTCCCTATGTTTTAAAGCTGGGGATCTCTTTTTCTGTGTCTAA  
TTATTTTCTCATTGGCTTGAAAAATCTGATAAAACATTTTAGGACTGTG  
TATAAAATAGAATTAGCCAAGTGCAATGTCTTTATTCAGAAGAAATTTCA  
TGGACGTTGTGCCTACTCTCTGGCTTCTGGCTTCATGGCTTTCCAGAT  
CCCACAGTAAGCTCTGGATAGTAGAAGTTATAGTAAGACTGACTTCTAAA  
TAAATGAAGTGACTTTAACCTTACTGATATGGCTTAAAGAAAAGGAGTGG  
CCTTTAAGATCCATGAACCTTCTCAAACAAAAGTGATAACGTTATCTCCAT  
GCATATATAATACTAAATATAATGCAACTGAGAGAAGTAGGCTGTGGTAA  
GAAAGGAGACCCAAAGTGCCATCTGAAGGCAGCACTTACCACCTCTGCTTCA  
TCCCACCGAGGAAACAAAGCATGAGTATTGCCAGATTTTCTTCTGTTTCA  
AGAAAAGCCAGAAATCCAGGTTTTTGGCGTGAATGTCTGATTTTAAATGT  
TGGAAGTAATTTATATTTTGAATAACATTGTGTGGGACAAGTGAACCTT  
GTATGTGGAACCTGCTTTCTCCAGTGGCGACAGTTTGGACCGTTGATAC  
TCAGCAAGTTCAGCCAAGTGCGCCTTGTCAATGTCAATCAAGGTGAT

FIG. 3 (18 of 52)

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GTGTGATTGGTCAAACAATTAGTTTTGCTCAGCATCTCGTGTGTTTTCA  
AGGACCTGAGGGTTCATTTGCCCATGCAGATCTTGTAGTCCTGTTTATTC  
TATTAATTTATCTTGCAAATCTATAATGTTTTATTTAAGCAGCGAGAGC  
CGTGGCAGCCTTTGGTCTGGACCCTTTCTAATGATCATTTAGTATCAGGC  
TATGTGGGAGTTGATTGTTTTGCATTGCCTGAAAGCCAAACAGTATCACTC  
CTCCTCTAGGTGTGGCAGAGATGTGAGAGAGGGAGACTGACAGTCTGTGG  
GTGTGTATGCAGTGTGTTGGGGGAAGCGAGGCACAGGGGACAATACTGTGGT  
GTATAAACTAGTCTAAGGTAGCATCAGGAAGTTCATGAAGCCAAAATGA  
TTTTTCATAACAGCACAAGACATTATTTGTTTTTGCCTCCCTCTCATTTTT  
TTTTTTTTTTGAGACAGAGTCTTGCTCTGTCTCATCCATGCTCGTGTGCAGT  
GGTGCATCTCGGCTCACTGCAACCTCCACCTCCAGGGTTCAAGCAATTC  
TCATGCCTCAGCCTCCTGAGTAGCTGATTACAGGTCTGCACCACCCCGCC  
GGCTAGTTTTTGTATTTTTAGTAGAGATGGGGTTTTGTAATGTTGGCCAG  
GCTGCCCTGTCTATTTTTTTTTACTAGTGTCCAGTGGAGTTTTTTAGGGG  
CTACATAACATGATACTGTCTAATTAATCTAATGGCTAATGAAAGGGATATG  
TATATGTTTTTGTGTTTTAAACAAACTTCTTTGGGGTCCCTCAATAATTTT  
TAAGAGTATAAAGGGGTCTGAGATCAAAGAGTTTGAGTCTGCTGGACT  
GGGACAGTGGTTGTCAACCCAGATTGTACATTAGGGTCTCTGGGAAGCT  
TTAAATAGTACTGATGCCCAACCTTACCGCAAACCAATTAAGCCAGAAT  
CTCTGTGGATGAGAAGTCTTCATTGTCTCATCATCACCATGACCATCATCAT  
TGTCACCGTCACTACACCATATCATCATCATCATATCATCTTCATTATC  
ATTGTTAGTATCTCCATCACCATCATCAGCATCACCATTATTATCATCAT  
CATCATCCCCACCATCATCCTCATCGGAACCTTCACCTGCATGGAGGACAA  
TCCACTATGCATTAGGTGCTATGCTATTTGCTATACTCCTTATTCTCACA  
ACTGCCAGAGAGGGCTGATATTATCTCACTTTATAACAGGAGGAATCTGG  
ATCGGAAAAGTTAAGGTAAGCTAATTCACAGAGCGAGAAGAGATAGAGCC  
AGGATTCGAAACCAGTTCTCTGCTACATCAATGTTCCAGTCTCTGCACT  
ATTGAGAACCTCTTTAGTTATGCTTTCACCCTCCAACACCACAGTAAAT  
TTTTCTTTTTTAAAAAAATTATCTTTAAGTTATAGGGTATATGTGCA  
TAATGTGCAGGTTTGTACATATGTATACATGTGCCATGTTGGTGTGCTG  
CACTCATTAACTCGTCATTTACATTAGGTATATCTTCTAATGCTATCCCT  
CCCCGCTCTCCCCACCCCATGACAGGCCCTGGTGTGTGATGTTCCCCACC  
CTGTGTCCAAGTGTCTCATGTTTCAGTTCACCTATGAGTGAGAACAT  
GTGGTGTGTTGGTTTTCTGTCCTTGTGATAGTTTGCTCAGAATGATGGTTT  
CCAGCTTCATCCAGTCCCTACAAAGGATATGAACCTCATCCTTTTTTATG  
GCTGCATAGTATTCCATGGTGTATGTGTGCCACATTTTCTTAATCCAGTC  
TATCATTGCTGGACATTTGGGTGGTTCCAAGTCTTTGCTATTGTGAATA  
GTGCCACAGTGAACATTCATGTGCATGTGTCTTTATAGCAGCATGATTTA  
TAATCCTTTGGGTATATACCCAGTAATGGGATGGCTGGGTCAAATGGTAT  
TTCTAGTTCTAGATCCTTGAGGAATTGCCACACTGTCTACCACAATGGTT  
GAATTAGTTTATAGCCCCACCAACAGTGTAAAAGCATTCTATTTCTCCA  
CATCCTCTCCAGCACCTGTGTTTTCGTGACTTTTTAGTGATTGCCATTCT  
AATGGCACCACAGTAAATTTTTATAGATTTTATAAGCAAATGTATTTA  
CTGTGCAAGAATTGGTTTTATTTTTTAAACCATGTGTGCAAACATACAAT  
GGTTAATTGTGATATTTGCTCAGTACAAGATCATCAGATCACTACACAGA  
CTTGAGGTAATTCACCTAAAAGCAAAGAGAACTGACCCACATTAACTG  
AGAAGTCTTTACTTATTTATTCCTATAAACGAGCCAATATGAAGAGAAG  
GCCTTAATGTGGTTAACTATGTAATTTTTTTCTGACTTTTTGAAATACTG  
AGAAGAGCTCATGACTCTCCCATCTCCTAATTCTACCTGGTGGATTTTA  
GACTGACCACAACCTCATGGGTAAATGAGGGAAGACGAATAAGAAACCTTG  
CTTTTTTTCTCCTTGTTTTTGGCTGGCTGCAGTGGCTCACACCTGTAA  
TCTCATCACTTTGGGAGGCCAAGGTGGGAAGATCACTTGAGCTCAGGATT  
TCAAACTGGCCTGGGCAACATAGTGAGACCCCATCTCTAAAAA  
AAAAAAAAAAAAAGGCGACAGGCGGTGCGTGCCTGTAATCCTACCTACTC  
AAGAAGCCGAGGTGGAAAGATCACTTGAGCATGGGAGGTCAAAGCTGCAG  
TGAACCTTGATTGCACCACTTCATTCCAGCCTGGGTGACAAAGCAGGACG  
CTGCCTCAAGAAAACAAAAACAAACCTTAATTTTTTGGCTATTCTTTTC  
TGGTAAGAATGGTATAGAGATGGGATGAGGATGGCTATTGTATGAGAGA  
GCAAACAGGGTCCAAGCAGTGCTCTGGGCTGTCTAAGGACCAGTAGTCAG  
CTTAACCTCTCAAATTTCCAGGGAAGGAGTTTCGGAGTGGTAGAATATCCT

FIG. 3 (19 of 52)

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GGGTATGCCCAAAGCATCACCTTGCAAATAGCCTGTCTATGAATAATTTG  
TTCATTTGTTATGACTGGAACTGGCTTTGTGTATGCCAGAGAATGGGGG  
CAGGAAAGAGAGATTGGTGTCTTGAGCTCTCTGTGCCTCTGGGGCAGTGA  
TGCTTTTCTCTCATGTGGAAGGAGAGCATGACTGAAAAGGTGCACAAAT  
AAGGTGTCTGTGAGAGAAATTAACCTTCCAGATACAGAGACACAACCTTC  
CCCAAGAGGTCTCATTTGCTCTGCCTTTTTCCTTTTTTTTGCTTGTCT  
ACCATTAATAACAGAACTGATTATGACCTCAAAGAGAGGAGAAAGCGA  
CTCTCCCCACCTAGAGCTAGTTAACCACCATATCTTCTAGATATCCTT  
GAGAGCAATGTAACCC  
>Contig29  
GTGAACTCGTTTTACCTGTGTAGCAGACCAAGCCGAGACAAAATCCNTC  
AGACACCAAATTAAGAAGGAAGGGCTTTATTGGGCCTGGAGCTGCGGCA  
AGACTCAGCTCTCCAACAACCGAGCTCCCCGAGTGTGCAATTCCTGTCCC  
TTTTAAGGGCTCACTACTTAAGGCGGTCCACATGAGAGAGTCTGTATAG  
ATTGAGCAAGCAGGGGTATGTGACTGGGGGCTGCATGCACCTGTAGTTA  
GAATGGAACAGAACATGACAGGGATCTTCACAGTGTCTTTCTATGCAAA  
TAACCGATTAGATCAGGGGTCTGATCTTTACCAGGCCCAGGGTGTGTACC  
GGGCTGTCTGCTTGTGGATTTTCTTCTGCCTTTTAGTTATTACTTCTTT  
CTTTGGAGGCAGAAATTGGGCATAAGACAATATGAGGGTGGTCTCCTCT  
CTTACCTGCGGGGAGTGAGCTCAAACCTCTTAAAGGAGTTACCTGCCTTC  
CATCATCAGGGAAGCAGGAAATCTTGCCTTCTTGTGGAAGCAASTAAA  
ACTCAAAACAAACAAAGAAAAAACAGGGAGTTGTACAGCAAAATAAACT  
TTTGATTTTGACCAAATTTTGGGAGATCAGGAATCTCTGAAGGAGATGC  
TTTCAGACCTCAGCAAATTTCTCTGTTGGTTTGAAGCCATAAAGTTAGCTC  
ATGCTGGTACCAACACCCAGTAGGAGATTTGTCAAAGGTAAGAGGCATCT  
CCACTCAGAATCCCTTCGTGGTTACCAACATGTGAACCTTGAAATCTGA  
GACAGGTCTCAGTTAATTTAGAAAGTTATTTTGCCACGGTTGAGGACAC  
CCACCCATGACAGAGCATCAGGAGTCTGACCATGTGCTCAGGGTGG  
TCTGAGCATCAGCTTGGTTTACACATTTTAGGGAGACATGAGACATCAGT  
GAATATATGTAAGATGTACACTGGTTCCTCCAGAAAGGCAGAACAACTT  
GAAGCAGGGAGGGAGCTTCCAGGTACAGGTAGGTGAGAGACAAACAATT  
GCATTCTTCTGAGTGTCTGATTAGCCTTTCAAAGGAGGCAATCAGATAT  
GCATTTATCAGAGTGAGCAGAGGGGTGACTTTGAATAGAATGGGAGGCAG  
GTTTGCCCTAAGCAGTTCCCAGCTTGACTTTTCCCTTTAGCTTAGTGATT  
TGGAGGCCCAAGATTTATTTTCTTCTACATCACTGTGGGCAGCTGACT  
AGGAAAGCTTTGTAGGACTGGTGGGCAGTGTGAGAGCCAGTGGGGGGTG  
GTGGTCTCTGTGCAATGGTAGCAACCACTGTGAGGCTGAGTAACTCAT  
TTCCCAACCTCTCTAGCAGCCCCAGTGGAGATACAGAGGAAGCAGACTA  
GCGATACAACCCAGCCTGAAGTTTTGTCTGGTGAAGTGAATGGAATAAAA  
ATGGGAAGGGTGCTGAAGAGACCAGCAAGAAAATGGTTGAAGAGATGGGG  
CACAGAAATTAAGCTGGATCAAAAAGGACGGAAGCAGAAAGGGCCGAT  
AGAGAGAGGGGATATCTATGGGTTCCGATTTCTGAAAAGGACAAATCACT  
GGTGTCTTTGAGAAGAGAGAGGGTGAGAAAGCAGGAAGGCTGGAGGCTGTC  
ATCCAAGAGGCGGACATCTGTGAACATGATTCCAAGAGTACCAGACCAT  
GGGGGTGGCCAAAGGGAGTGCCTCTTCTCACTCTTACTCTTAATTCCTT  
GTACTCAAGATAATAAGTTCCCAGAGAGAAGTACCCATATTTAATTCAT  
CTGTGTCTTCTAGCAGTACTAAAAATATTATATGAAAGGTATCAAACCT  
TTGAGAATGTGTGCTGCTAAATTTGTTAAGGATGCTGGAAAACCTCAAGACG  
TCCCTGATCCTGAGCCTGAGTATGAGCCTGTGGTGAGCCCAATGCAGGTC  
TCCATTGAGACAAAGGCCTCAGGGAACGGATGAGACCTAGGGACAGAGAT  
GCATGCTGGAGCAGCATTTCCCATCTTACTGCAGCTCAGGCCAGCTGAC  
TGCTTTATGAGTAAACGTTACCAGGGAACACTTTGCAGTCTTAACACACA  
TGCCACCTGTGACCACTGATCCCTGTTGGGTGACCACTGACATCAGAGA  
TTCGATGGCAGCAATGAAGACAAGGCTATCCTCATTAGGAAGGAAAGGAA  
GGAGGAGGGAGGAGGGCAACGAATCTTCTCTGCTTGTCAACCACGTCCA  
TCTCTGTTAGGTGATTTCCCATGTGTGACTTTGTTTATCTTTATAATAAC  
TCTGAGAGGTAGGTCTTGATGTCCACATTTTGAACATGAGGACATCCAGC  
CAGGAAGTTGAGTTCTGGGACATAGCTGAGAGGGCAAAGCTACATATAA  
ACCCCTCTTGTCTTTTCTGGCTTATCCACTGAGTGCCCCCTGCAATCCA  
CCAGCCCATTTGTGAAGTGCACTATAGGTAAGTTGGCACAGGAGGAGT

FIG. 3 (20 of 52)

GGATGTGGGCGATTTTG. CACAGCTCTCCAGGAACCTTACACACTGGTGAG  
GAGGGCCAGGTATGTTCCCTGACCAGTCACAATCAAAGCAACCTCCTACTA  
ATCAGGGAGGCTTGGTACCTGGGGAATGCTATGTTGAAAGGTTCTTTTCT  
GGGTTTTAAATGATGGGTCTATTTCTTATTCTTAAGATTGCTTTTTTT  
CTGGCTAGAACTTAAAAGAAATTTTTCAGTAAATTTCCCTTCCCTGGGCAC  
AAAGTGAGCTTGAAATGAATTTCCAGGTGGCCTTGATACTTTAAATATT  
GCCTCCTATAAAATCAACCTTTAGAAGAAGGAAGTCAAAGAACATGCTAG  
ATTTACAAAAGGTTAATTCCTTGAAATCCAGTTATCTACAGGACAATGTT  
GTCAAAGAAAAATTATTTGGCCAGGCACGGCGGCTCATGCCTATAATCC  
CAGCACTTTGGGAGGCTGAGGCAGGTGATCACCTGAGGTGAGGAGTTTGA  
GACCAGCCTGGCCAACATGGTGAAACCCCATCTCTACTAAAAATACAAAA  
AAAATTAGCCAGGTGTGGTGGTGGGCACCTGTAATCCAGCTACACGGGA  
GGCTGAGGCAGGAGAATCGCTTGAACCCGGGAGGAGGAAGTTGCAGTGAG  
CCAAGTTCAAGCCACTGCACCCAGCCTGGGCAACAGAGCAAGACTTTGT  
CTCCAAAAAATAAAATTTCAATGATATTTTAAATTCATGGTAAGGAA  
GATTTTCAATCAGAACCAGCACAGAAGATATAGGAAACACTGCAATGGGAC  
TTTGCGGTGGGGGAGAGAGATTGAACACAACCTACATATACAGCACGGGCA  
AGGACATATTCATAGCCAGGAAGCAGAGCAAAGATCAGTGGATGCGAAAT  
TACTAAGAGGAAACATGAAAAATAAGGGAGCTTCTGCCTAAACCCACCTA  
ACCGGATCCTTGCTGAAGACAGGACAGGGTGATTGGACACCACTTTGGGG  
ATGGTGGAGGATGGGGAATCCAGTGAGATTTCAAGGGTGATGCGAATTG  
AACATACAAAGTTCTTGCTAAAAAAGGATTTTACAAGAAAGTGACAAAT  
GTGCTTGGGACAAGGTGCAGGAGCCCGACGGAGATGTGGTCCAGCAGAGA  
ATATGTGCGGAGATGATAGGTGAGTTCTCTGACGAAGGATATATGCTGAT  
CCAGCCAGGGTGAAATGCTCAGAGAAAGCACGGAGGGGCTATGTCCGTTG  
CCCCAGTCTCCACGGGTCAAATCTGATCCCGTTGTGAGTGTGGCCGTTT  
GTAGAAAGCAATCAGGGGGGTCCCTCCCC

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AATATATATTTTTTATANNATNTGAGACAGGTTCTCACTAGGTTGCCAG  
GCTGGTCTTGAATTCCTGCCTTCAAGTGACTCTCCACCTTAGCCTACTG  
CATAGCTGGGATTACAGGCACAAACCACTGCATGCAGCTAACTTTGCTTC  
TCATTCAGCACTTTTTATTCCACTGATTATATGTATATGTATATCTGCA  
TCATCTCTCTCTCTCTCTCTCTCTCTCTCTATATATATATATATAT  
ATGGAAATATCTCTCTCTCTCTCTATATATATATATGGAATATATATCT  
CAGTCTCTCCTATCCTCTTAAATCAGTTTTGCTATCCTGTCAATCCCC  
CAACGAGTGTGATGTTGTGAAATATATATTTGTTCTTCATCTCCTGTTTC  
CTGACATACAGCTTTTAAAAACCCCTGGAATCTCTGGAATAATAAGAGTG  
TCTTTTGCATGCTAATAGATGACTGCTGGCTGGCAGCCCCAATGCAGTAG  
CTTCATGATGGGGTTTGTACAGGAAAGACCAAGGCAGGATTGGAGACTT  
GAGACTGTTAGCCCCACTCCCCAACCACTGGAGGGAGTGGAGGGGCTGAA  
GGTTGTGTGAGTCACCAATGGCCAATGGTTCGGTCAATCATGTGTATGTA  
ATAAGCCACTCTTAAAAACCCAAAAAGGACAGGGTTTGAAGGGCTCCC  
AGATAGCTGGACACATGAAGGTTTCTGGAGGGTGGTGGCCAGAGGGGCA  
TGGAAGCTCCACACCCCTTCTCACATGCTTTGCTCTGCGCATCTCTCAT  
CTGGTGTTCATCTGTATCCTTTGTAATATCTTTAGAATAAACTGGTAAA  
CTTAAGTGTTTTCTGAGTTCTGTGAGCTGCTCTAGCAAATTCACGGAAC  
CCGAGGGAAGCAAACCCAGATTTATAGCCATCAGTCAGAAGCATAGGTGA  
CAACCTACCACCTTGTAACTGGCACCTGAAGTGGGAGGCAGTCTTGTGAGA  
CTGAGCCCTCAACCTGTGGGATCTAACGCTAACTCCAGGTAGATAGTGT  
GGAGTGAAATTAGGACACCCAACTGGTGTGCGCTGCTGGAGGACTAGTGGT  
GGGAGAAAATCCCCAAGCATTTCCGGTGACTAGAGGTACAGAAGAACTCAG  
TGTTGAGGTGTTGTGACAGTATGGTAGGGAAAACCTGCGTCTGGTTTTTTC  
CTTTTACAAATCAGTTAAATATTTAACACAAGTCTACTGTATATTAGTAAA  
AGGGTTACATTTTTTAAATGTCTTGACAGTTGCACTTTGACAACCTCCATA  
TCAATCACTTTTTTTCGTGTCCGTTTGAACCAAATCACTTGGGATACC  
ATGAACAGGCTGCAGCGTATTTCCCAAGGCCTTGAAAGCTTGGAGGCCAT  
TTTGGCAGCCNTAAATCCCTGTGAATACCAGGCTTCGTGGATTTAAAAAT  
AGACTTGAGGCCAAGCCCTGGTGGCTCACACCTGTAAGCCCAGCACTTGG  
GAGGCAGAGGCGGATAGATCACAAGGTTAGGAGTTGAGAGCCAGCGTGGC  
CAACATGGTGAAACCCGCTCTCTACTAAATATACAAAAAAATTAGCCG

FIG. 3 (21 of 52)

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GGCGTGATGTTACACG CAGTAGTGCCAGATACTCAGGAGGCTGAGG CAG  
CAGAAATACTTGAACCTGGGAGGCAGAGGTTGAAATGAGTCAAGATCGTG  
CCACTGCACTCCAGCTTGGGCGACAGAGTGAGACTCAGTTTTTCAGGGGAG  
TTAAACAATAACAAAAAAGAAAAAGACTTGAACAATGAGGCTCCACTGG  
ATGGATTTAGGGGAATTACAGGAAGCAGGACCTGACGGTGCAATGCCACA  
CTCCACCTGTCCAGAATTGGACCTCACCAGGGAGGTCTGTGGGGACAGG  
GAGAGGCCCTCTGCCTCCACCCCTCCTCTACTCCCCAACCTTGAGTCA  
GGCTGAATGTAGTAAACCTGGAACAGAAAAGTTCAGTTTGGCAATAGGTA  
TCTGAAGGACTCCAGGTGCTTCTCCCTTGATTCAAAATTTTACTTATAAA  
AAAAATTATAAGAAAATTCTACTTAAAAGAAATAATCAGGGAGGTACAAC  
AAATTGTACTTTTTTTTTTTTTTTTTTTTTTTTGGAAATGGAGTCTCACTG  
TTGCCCATGCTGGAGTACAGTAGTGTGATCTCGGCTCACTGCAACCTCCG  
CCTCCTAGGTTCAAGTGATTTTCTACTTCAGCCTCCCAAGTAGCTGCGA  
TTACAGGTGTGTGCCACCACACCCGGCTAATTTTTGTATTTTTGGTAGAG  
ACGGGGTTTACCATTGTTAACCAAGATGGTCTCGAACTCCTGACCTCAGG  
TGACCCACCTGCCTCAGACTCCCAAAGTGTGGGATTACAGGGGTGAGCC  
ACTAAGCCAGCCATTGTACATATTTGTGGGTATTTACTAAAACATTAT  
TCAAAATAGTAAAAAAAATTGAAATAAACTGGGGACTGGTTAAATAATT  
TTGGGTACAACCACATGATGGAATACTATACAGCCATTAAAAATTACATT  
GAGGCCAGGTGTGGTGGCTCATGCTTGTAACTTAGCACTTTGGGAGGCC  
AAAGTGGGAGGATTGCTTGGACCCAGGAGCTCAAGACCAGCTTGGGCAAT  
GTGGCAAAACCTGTCTCTAAAAAAAATAACAAAAAATTAAAAAGCT  
GGGTGTGGAGGCACACACCTCTAGTCCAGCTACTCAAAGGGCTAAGGTG  
GGAAGATCACTTGAACCGGGGAGGTCAAGGCTGCAGTGACCCAAAATCGG  
GTCAATTGCACTCCAGCCTGGGCAACAAAGCAAGACCCTGTCTCAAAAAA  
AAAAAATACATTGAAGAATATCTTACGGTATGGATAAATATTCATTTTA  
CAGTGATAGATGCAATAAAAGCAAATTACAAAATATACAGTTTAATTCC  
AACTTTGATACTACATATGTATATATGAATACATGCATATGTTATGTATG  
TATATGTAATATAACAATATATGTCTCTATATATGGATATTATATATTTA  
CACATACATACACATATATAATATCTTCTCTAGAGAGCAGAAAGAGAG  
TAGACAGATAATGAAGATAGGATACAACTCCAGTCCAGCTCAACCTAGGG  
GACTTGTTTTTAAAGCCTCAGGAGAGAGAAGTTGGGACTAGAAAGCAAGGC  
AGCTATTTGTAAAGCATCTTTGTGTTTCATGCTATTGGGGTGGGAAACAAC  
AGCACAACTTTTGAAGGCCCTTTCTACTCACCCCAAACTGCAGAGCA  
GCTTTAGGACCCTCAGAGTTCAAGAAGACCATTTCAGAGTAGAAGAAGT  
AAAAACATGTATGAACCTGACCCCTGAGCTCATGGACTGTGCCATGAGGGA  
AATTCTTAAAAACAGCAGGAGAGGCCCTGGAGGAAGGCAGAGGCCCTGCAT  
CAGCAAGTCCAGGCAAAAGCCTGCATTCCATAGATGCTCATCTCTCTGGC  
TGGTGAGGTCTAAAGACGTTTGGTCTCAATATTAAGTCTCTGAGAGAGG  
TCACAAACCCAGTCCCTTGGCCACAAAAGGAAATAAATCTGGCTTGAGA  
CATTAGGGAGGAACAGGGCAAGGGGAGGTTCAAGAAAGTTTTAATGGATG  
AGATGATATTTAAGCAAGGCCCTGGAAATGAGAAATTCACCAATAGCC  
ATATGGTAGGTGAGAAAGCAAGATAAGGAGGGGGCAAGTGCAAGGGGCA  
ACATCAGATATGACCAGGGTGTCTGTGGGCATGGCTGATGGAGAAGAAGA  
TTAGACTGGAGTTTGGGAATGCCACAGTATCGAGGTGGATTTAATCCTA  
TGGGTAATAAAGCCAACTGTTCAACCCCCAACCCACTTGCAATATGGCTC  
CAAAATAGCAGGTGTTTGATAAAATGACTACTTTTACTCTACTATTCCCT  
CCCTCTTAAGAAGAAAAAGAAAGTGGAGGCTCAGAGAAAGGCAGTGGCTT  
GTCCCAATCACACTATGATTTGGCCACAAAACAAGAACGAAATGTTACAC  
CCAAAAATGCTGCCTCCACCTCCCTTCTTGCTTTCTCCCTGCTGGACT  
ACAGACTATCTCAAGAGTGACGTACACCATCAGGGCTTCAGCTTTTCCCC  
GAAACAAATGCCAAATATTAGCCATACGTCACTGTAGTAAGAGCCCTGAA  
TTGGGAATCCAGCTTTGACGCAGACATGCTGATTGACTCTGTGACCATT  
CTCTTCACTTCTCCACTCTATTCTTCCCCACCTGTAAAGTGAGGTCTTT  
CCAGTTATAAAAACAGATGATGCTATTGTCTGTTTTGTATCTAATCTTG  
CTGTGTTATAAAAAAAAATAAGGCTCTGTACATTCACTTGGCCAATTC  
CCTTCTTATCTCTACTTCCCACAGCCCTTTTCTACAGAAAACCAGCAT  
TGTTCTTCTGGATCCATCTCTTAAGAAAGCGCTTTGCCCTCCCGGTTATT  
TAGGTGATAAGAAGTGTCTTAGATGACAGCCCTGGAATGGGCTGGAGGCA  
ACAAAAAGCAAGTGAAATAGACAGTTACAGCGACGACAATAATAACAAC

FIG. 3 (22 of 52)



CAACACCTCTCACTAAAGAGAAAGAAATAAAAAAGAAAATTAAAATCTGC  
CGCAATGCCACACAGTCATTGAATAACTGCATGTGTACAGCACTTGGTT  
ACTTTTACATACTTCATATTTTAGCCTTCATAGCAGCTCACAGGGGTGGA  
TTAATTTTGTAGTCCAACTCCTGTACGGTGCCTGGCACAAGTATAATAA  
ATGTTCTGTGAATAAATGACCCTCTTTTATAGATGAGGAAATCGAGGCTCA  
AGGAGAACAAGCAATGTAATGTCCCCCTCCTGTTAGCCATCTGCCTTTC  
AGGCCACTGAATGCAGTAGTCCTCAGTGCCCTGAACTTGACCCTCTTCTG  
CTTTTCGGACTGGTCTTCTAATCCCGTTGTGACTCACTACACCACCTCT  
CCTGCATATGACATCTACATTTTAAAACAAACCGTATGGAAATAACACAT  
TAGTGGGCTTGTTCCTCCACCCCGCAAAAAAAGGCTCTTTATAACA  
GAACTTCTCAGGCTGGTAGGGGAATTTTATCCCCCATTTATGGTAGAA  
AGGCCCTAACCTTGGACCTCAGCCATAGCTATTCACATGGGGGAATGAT  
GAATAACATGGGGAGCAGCATGTAAATATCATTGAGCCGTAGTCCAGACC  
TATAACATC

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GGGGGAGCTGCATGTGCCTGTGCGAGATCTGGGGGAGGAACAGGAAGATCA  
AGAGTTCTGTGTAGGACATGTTAAGTTGAAGGTGCTTACAGGATAGCCAG  
ATGAAGCATCAGGTGTGCAGTCAAAGATATGAGTCTGGAGCAGCACATCC  
TAAGTCACCTCCTGCACCAACACAGAACTCCAGGCCACTCACTTGAGCT  
CTCCCAAATAGTTTCCAAGTGTCAATTATGTTAATAACCTATGAGCTTGAA  
CACCAGATTCAAACCCCACTGCATGGCTTTTAAAGACCATCTCAAGGGCT  
TGACACTCCAGGGAGCCAACTAAAGATGCCTGGTCTTACCATCAACCTCC  
ACCCCATTTTTTATAGAAAATGTTTCTACCTGTCTAAGGCAGGGTCTG  
CCCCACTCCAGGCCCTTTAGATCCCCAATATTCTCTCTCCCTGAACCA  
AAACCTCATCATCTTCCAGCATGGGTGGGGCTCCATTCTTGCTTCTGC  
TCCCTGAGCAGAAGCAAGTTTCTCCCACTTGACCTGATTCTCTCTCTA  
AGTACCAGTCACTGCTTTGTTTCTGGAATGAGAGAAAAAGACAGAGTGAG  
AGAGACAATCCAGAACTCTTGCTCACTCAGCTAGGCTGGGCATCTGGG  
AGGATGGCTGTGTCCATGGGAACCTGGGAAAAGCCACACCTTGGCACCC  
TGGTCACCCACCTGTCTCCCTGGCAGATTCCGCACTGCTCTCTTGACCC  
TCTACCAGGGCTAACCGGCTGCTCACTCTCCCAAGCATGTCTTCCACG  
CCCCTCTCTAATTATTACATTCCCTTCACATAAACTGCCCTTCTCTCC  
AATCACCACATGTTCACTTCCCAACCCAGCTGTCAAAGTCTGGCTCAACCT  
CATTCTTGAAAAGGAAAAAACAACAAACAACAACAACAACAAGCAAAAA  
ACCTATGATGGATTAAGAACACACTTCATTCCAGGAACATGCTTATCTCC  
CTAACTCTCACAACAACTACAGCAGGTAGGTGTTATCACACCCATCTCT  
CAGGTGAGAAAACAGGCTCAACGAGTGCAGGAGGACACAGCAAGTCAGTG  
ACAAAGCTTAAATTCAAGCCCAAGCCTGTTGGCAACCAACGTCTGTACCC  
TTGATAGCTACCTCATTTACCACCAATCCAGTGGCCTCAGGCCCTGGCTG  
CACACTGGGATCACCTGGTGCCAGACCACATCTTAGACCAGTCATACAG  
AATCTCTTGGGCTGGGATCCTCCACGGTACATTTTAAGGGTCCCAGGTG  
AGTTCCACCATGGACCCAGAATTGAGGACCCAATACCGTATACCATCTCC  
TTCTTCATCTCTTCTAAGGCATCTCTTACTCGCTGTGCACTCCCATACCA  
CTTTGTTCAATCATCCAATCATTCAATTCAATTGAGTCAGTTAGTCAGGAGC  
TACTCACTAGTCCCCTGCCAGGTCTAGTCATGACATAGGGCTCTGGGGA  
CCAACAAGAAGCAGGACCCATGCCTCCTGCTCTCATGGAGCTTGCTCTGC  
AGCAGAGGAAGCAGTCAGTGAGATGTAGCAAATGTGAAATGTGCACAGAT  
GGGAAAAGCAAACTTTAAAACCTTTTAGGACAAAATACACAAGAAATCTT  
TGCAACTTTGGGACAGGAAGGAACAACATTCCTTACACATGACACCAAAG  
GAATCAACCATAAATAAAAAGGTGATCAATTTGACCTCATTTAAGTGTTA  
AGCTTTTTTCAATTGAGAGACACCAATAAAAATTAAAAATACATGCCACAA  
ACTGGGATACAATATTTACAACACTTATGTCTCACAAGGATTAGTTTTTC  
AGAATATATAAAGAACTCCCGGCCGGGTATGGCCGCGCACGCTGGAATCT  
CAGCACTTTGGGAGGCCAGCGGATCACATGAGGTGAGGAGTTCAAGACCA  
GCCTGGCCAACATGGCAAACTCCGTCTCTACTAAAAATACAAAAATTAG  
CCAGGCATGGTGGCGGGCGCTGTAATCCAGCTACTCAGGAACTGAGG  
CAGGAGAATCACTTGAGCCCAGAAAACAGAAAGTTGCAGTGAGCTGAGCTC  
ACATCACTGTAAGCCTCGGTGACAGAGTAAGACTGTCAAAAAACGAAAA  
CAAAAAACAAAACTCTACAAATAAATAAGAAAAAATAGCCCAGCAGGA  
AAAAGTATATACATTTCTAAAAAGAATAAATACATTCTGTCAGTTTTCTA

ACATATATTTTTTAAGAGTAAATACAAATGGTTAGGAAACATTTTTTAAA  
ATGCCCAACCTCATTAAAAATTATAGAAGTGAATAAAGCCACAATAAG  
ATACGATTTTATACCAAATACAGTGTCAACACTTTGCAAGTCTGACCTCA  
CCAAGTCTTACCAGACGTGTGCACTGACGTGGCTGCTGAGATACTGATGG  
TGGGTCTGTAAATCTGTACTACAAACAATTGCAATAAAATGTAATAAATA  
TACAATAGGTGGAGCAGGAAGTGACCTGCAACCATATAGCAGATAGGGCA  
GGAAAAAGCCTATGAAAGCTGACATCAAAGGGATAAGTTCAGTTACCCA  
GCTGAAGGGAAGGAGGGTGTTCAGATAGAGGAAGGATAAGCATGACCTA  
TTCAAGGGCAGTGAAAGAAGCGTGCAACGGCCAGTCAGGAGAACCTGAA  
ATTGTGTCAAAGAGCTTGGATGCAAAGAGCCGTGGGAGACTATTGGGGGT  
TTTAAGCAGGGATATAATATTCAATCAAGCATGCAGTAAAAGGTCACTGG  
CACCTGCCATGGGCCAGGACTCGGGCTCTACATGATTGCGTCTGTTTTGG  
AAATATCACCTCGGCTGTGAGATGAAGAACAGGTAGGAGGGTCACAAAC  
TTGAAGCAGAGAGACTGTTGAGGAAGTAAGCTGTTTTTGTGTGGACTGTG  
GCAATCACAGAGGCAGAGGATATAAATGCACAGAGACACAAGGCATGTGG  
GAGGCAGAGGAATCAAATACAATGAGTGATCAGATGTGGGGTTAGAGTG  
GTGAGTGAGAAACATACTCAAGGTGACACGCCAGGTATCTGGGTGGAT  
GGTAAGACATTCATGGACTAGGATCGAGGAANGAGGTGGGGAATGGGACC  
ATACCTGCAGTTTATAAGGGGTGGACGAGGGAAGATTATGCGGGAGACTG  
AGAGAGGAATAGACAAAGGAATCCCGGTGCAGTATTACAGAACTGGGGT  
GGGAGGGGGTTGTANTTCAAAGGAAAGAAAATTGTCAAATAGTATGAA  
ATGCTGCAGAGAACTCACGGATTTTTTTTTTAAGCTTAGAATTATTATCAT  
TGACTATGTGAATAAGAATAACTTTTATGAAAGAAGTTTTGCTTAAGTAG  
TAGGAAGAAGCAAAATTTGTTGAGGGCTGATGAGTGGGAGGAGAAGTAATT  
GAAGGCACTCTTTCAAGAGAAACAAAGCAGAAGGTGAGGAGAATACTAAT  
GAAGGAGTTACGGCCTTCACTATTTTTGTTTTGCTTTAGATAAGCAAGACT  
TGAGTGGGTCTGGTGAGGAGAAACAAGTAGAGTACAAAGTTAAAGGAGAG  
ACAGACAGAGATAGAGATAGGGACAGAGAGAGAGACAGAGACAGAGCACA  
AAAGAGCAAGGTCCCTGAGAACACGGGCCTTCTGTTTTAAACCCAGCCAG  
ATGTATTGCAATTCAATCCAGTACTAACCACCCAGAGTTTGTGTAGACT  
CTACAAGTTAAAGAGCATGGTCCCAACAGACTGCTTCTACGTCAGATG  
CCAGGCACACTTCAGGGGTCCCCAAGCCACTCATGTTTTTTGAATGACTG  
CCATAAGTTCAAATAATCCCAATTTCTCTCAGATTCAATAACTGGGTAT  
AACCACCTCATAGAACTCAAGAAAATGCTATCATTATTATTACAATTTTAT  
TATAAAGGATACAAATCAGAAGGACTAGCCAAATGAGGAGACACATAGAG  
AGAGGACTAGTAAAAAACAGAGCTTCTGCGTCTTACCTTCAAGGAATCAG  
GATGCACCAACCTCCAGCACATCAAGTGCTCATCAACCAGGAAGTTCCCT  
CTGAGCTCCAATGTCCAGAGATTTTAGGGAGGATTCAATACATAGGTATC  
ATTGATTAAATCATTTGGCCATGTACTTGAACCTCAATCTCCAGTGTCCCTC  
TTCTCCCTAGAGGTCTGAAGGGTTGGCTAATATCATGTGGCTCAAAGCCC  
CAACTCTAATTACCTTTTTTGGTCTTTTCAGGGACTAGACCCCATCCTGAA  
GCTATCTACAGGCCCTGCCATGAGTTAGCTCATTAAACATAACAAAGACAC  
TTATATTACTCAGAAAATCCCAACAGTTTTAGAAGCTCCATGTGAGGAAC  
CTGGGACATAGATCAAATCTTTTTTTTTTTTTTTTTTGGAGACAGGGT  
CTTGCTGTGTTGCCAGGCTAGAGTGCAAGGACAGATCACAGCTCAATGC  
AGCTTCAACTTCCAGGCTTAAGTGACCTTTCCACCTTAACCTTCCAAGT  
ATCTGGGACCACAGAAAATGGCTAATTATCCTGGCTGATTTTTAACTTT  
TTTTTTTTGTAGGGATGGGATCGCCCTGTGTTGCCAAGGTTGGTCTCAA  
CTCCTGGGTTCAAGCAATCATTCTGCCCTGGCTCTGTGATGGTTAATAC  
TGAGTGTCAACTTGATTGGATTGAAGGATACAAAGTATTATTTTGGGTG  
TGTCTGTGAGGGTGTGCCAAGGAGATTACATTTGAGTCAGTGGACTGG  
GAAAGTCCACCTTTCCAGTGACTGGGAGACCCACCTTCAATCCAGGT  
AAACACAATCTAATCAGCTGCCAGTGGTCAGAAATAAAGGAGGCAGAA  
GAACAGGGAAACACTAGACTGGCTTAGTCTTCCAGCCTACATCTTTCTCT  
CATGCTGAATGCTTCTACCTCGAACATCAGCCTCCAAGTTCTTCAGTT  
TTTGGACTCTTGGACCTTCAACCACAGATTGAAGACTGCAGTGTGGCTT  
CCCTGTTTTTGAAGTTTGGGACTCAGACTGGCTTCTTGTCTCCTCAGCT  
TGCAGATGGCCAAATGTGGGACTTTAACTTGTGATCATGTGAGTCAATAT  
TCCTTAATAAACTCAGATATATATATATGTATCAGACATATATATATATC  
CTATTGTATATTATATACAGATATATAATATCCTATTATATACAGATATA

FIG. 3 (24 of 52)

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TAATATCCTATTATATACAGGTATATATATATATATGTATCATATATA  
TATCCTATTGGTTCTATCCCTCTTGAGAACTCTGACTAATACAGCCCTCCC  
AAAATGCTGAGATTACAGGAGTGAGCCACAGCCACCATGCCAGCCSCAA  
ATTCTTAATTATACAACATGGGTCCAGAGATCAGGGCCTGGGTAGGATG  
CAGCAATAAGAAAAACAGATGGTGGATGGGGACACATGTTGGAAGTGTGGC  
AGGACATGGCTGAGGGAACTCATAGGATGGTGTCTATTTTCATGGCTGAG  
TGTGAGGAACAGCATAAAGGTCAAAATTTTCAGGTCAATGGTGAGTTTTTA  
AATTGTTGCTGTGAACCCCAAAATCTGACCCAGGTCTCAGTTAATTAG  
AAAGTCTATTTTTCCAAGGTTGAGAACACCCACCCACTCACGACAAGAGC  
ATCAGGAGGTCTGACCACATGTGCCCAAGGTGGTAAGAGCACAGCTTGG  
TTTTATATATTTTAGGGAGACGTAAGTCATCAATCAATATATGTAAAGATG  
TACACTGGTCTGCTAGAAAGGCAGGACAACTGAAGCAGGGAGGGGGC  
TTCCATGTACAGGTAGGTGAGAGACAAACAGTTGCATTCTTTGAGTTTC  
TGATTATCCTTTCCAAAGGAGGCAATCAGATGTGCAATTATCTCAGTGAG  
CAGAGGGATGACTTTGAATAGAAAGACAGGCAGGTTTGCCCTAAGAAGTT  
CCCAGCTTGACTTTTCTTTAGCTTTGTGATTGGAGGCGCCAAGATTT  
ATTTTCTTTTCAATTTCCCCCTTTCTTTTAAGAATCTTTAAAGAA  
AGCTTTTAAAAAGAAAATGAGTCTCTGGTCCCAGGTTTCATCTGAATTCT  
CGAGGGGAGGATGGTTTATCCTAAACGGGTGGTTCTGAATTTTGAGAAAG  
TGCATTGTAC  
>Contig32  
AAAAGCCATACGAATGAGGAAGAATTAAGGGCCAGAACAAAAACAAGAAGA  
TGAGGGAAAGTTTGAACCTTTAGAGACTGGCTAAATGGTGTGACCAA  
AATGCTGATAGTGATACGGACAATGAAGTCCAGGGTGACAAAGTCTCAGA  
TGGAAATGGGAATTTGTTGGAACTGGGCAAGGTCAACCTTGCTATGA  
CTCAGCAAAGAAATTTGGGTGCATTGTGTTTATGTCCTGGGGATCTGTGGA  
AGTTTGAATGTAAGAGTGATGACTTACGGTAGGGTATCTAGTGAAGAAA  
CCTCTAAGCAACAAAGTGTGTTGCTTAGAAATTTCTTTCTTTCTTTTTT  
TTTTTTTTTGAGCTGGAGTTTTGCTGTGTGCGCCAGGCTGGAGCGCAGTG  
GCGCAATCTTGGCTCACTTCAAGCTCTGTCTCTGGGTTTATGCCATTCT  
CCTGCCTCAGCCTCCCAAGTAGCTGGGACTACAGGCGCTGCCACCATAC  
CTGGCTAATTTTTTAGTATTTTAGTAGAGACGAGGTTTACCATGTTAGC  
CAAGATGGTCTCAATCTTCTGACCTCGTGATCCACCCGCTTGGCCTCCC  
AAAATGCTGGGGTTACAAGCATGAGCCACCCGCTGGCCTGCTTAGAAA  
TTTCTAAGCCAGGATATGGCCTGTCTGCTTCTAACAGCCTGTGCTCAGGG  
GTAAAGAAATGACTTAAAGTTGGAACCTATGTTTAAATGGAAGTAGAGT  
CTAAAAATTTGGAATTTGCAGCCTGGCCTTGTGGCAGAGAAAGAATCC  
AAGTAGGCTGCAGAGCAATCATTGCTAGAGAGATTAGCATGACTAAAAGG  
GAGCCAAGTGCTAATATTCAAGACAATGTTAAAAAGGCCCTTGAGGGCATT  
TCAGAGATCTATGAAGCAGCCCTCCCATCACAGGTGCAGAGGTTTGGTG  
CACTAGGCCCAGAGGTTTTATGGGCCANNGCCAGGGCCACACTGCTATGC  
ACAGCTTTGGGACACTGCTGCCCGCATCCAGGCCACTCTGCTCTGGCTCC  
ACCTTTGGCTCAAACGGGCCAAGATAGAGCTTGGACCACTGCTCCCGAGG  
GCACAAGCCATAAGCCTTGGTGGTTTCCATGTGGTGTAAAGCCTGCAGGT  
GCCCAGAATGCAAGATTGAGGGAGCTTGGGCACTTCCACCTAAATTTAG  
AGGATGTGTGAGAAACCTTAGGTTCCAGGCAGAAGCATGATACAGGGGC  
AGAGCCCTTGACAGAGAACCTCTACTAGGGCAATGCCAAAGGAAAATGTGG  
GGTTGGAGTCTCACACATGGTCCCCACTGGGGCACTACCTGGTGATACT  
GTGGGAATGGGGCTGCTGCCCTCCAGACCCAGAATGGTAGATGCACTGG  
CAGCTGGCACCCCTGAGCCTGGAAAAGCTGCAGGCACTCAACTCCAACCCA  
TGAGATCAGCCACATGGGCTACTCCAGGGAAGCCACAGAGGCAGGGCT  
GTCTAAGGCCTTGGGAGCCTACCCCTTGAACCAGCTTGCAGGACATGGAA  
TCAAAGATTATGTTGCACTTTAAGGCTTAATGTTTTCCCTGTCAATTTT  
AGGCTTGTGTGGGACCTGTTGCTTTTTTTTTTTTTTTTTTTTTTTTTTGGT  
CACAGGTGTTTGAACCAGAACATTCATCTTGAATAGGGGCTGGGTAAA  
ATAAGGCTGAGACCTACTGAGCTGCATTCTAGGAGGTTAGGAATTTCTAA  
GTCACAGGAGGAGATAGGAGGTCCGCACAAGATACAGGTAGCGAAGACCT  
CGCTGATAAAATAAGTTGCAGTAAAGAAGCCAGCCAAAACCTCACAAAGCC  
AAAATGGTGATATGGTTTGGCTCTATGTCCCCACCCAAATCTCATCTCAA  
ATTATAATTTCCATAATCCCCACATGTTGAGGGGAGGACCTGGTTGGAGG

FIG. 3 (25 of 52)

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TGATTGGATTATGGAGGCAATTTCCCCCATGCTGTTCTGGTGATACTGAG  
TGAGTTCTCATAAGATCTAATGGTTTTATAAGTGTGGGAAGTTCTCCT  
ACACACATGCTCACACTCTCTCCTGCAGCTTTATGAAGAAGGTAAGTCTGCT  
TTCCCTTTCTGCCATGATTGTAAGTTTCTGAGGCTTCCAGCTATGCAGA  
ACTGTGAGTCAATTAACCCGTTTTCTTTATACATTACCAGTCTTGGGCA  
TTCTTTTACAGCAGTGTGAGAACTGCTGGCGATGAGAGTGACCTCTGGTT  
GTCTCAGTCTCATTATATGCTAATTATAATGTATTAGCATGCCAAAAG  
ACACTCCCAACCATGACCCCAACAGTCATGCCTGTGCCGGTCTCAGCACCA  
TGACAGTTTACAGATGGCATAGCAACGTCTAAAAGGTACCCCATATGGAC  
TAACAAGGGGAGGAACCCCTCAGCTCTGGGAAGTGCCTACCTCGTTCCCG  
AAAGCTTGTGAATAATCCACTGCTTGTTTAACAATATAATTAAGAAATAAC  
TATTAAGCATCCTTAGTTTACAGCAGCCCAAGCTGCTGTTCTGCCTATGGAG  
TAGCCATTCTTTATTCCGTTACTTTCTTAATAAAATTGCTTTTACTTTAC  
TGTATGCTACTCGCTGGAATTCTTTCTTGTACGAGGTCCAGAGCCCTCTC  
TTGGGTCTGGATCGGGACCCCTTTCTGGTAACATTTTGACCAATTTCTCC  
CTTCTGGAATGGGAATGTTTACACAATGACTGTATCACTTTTGAATCTTG  
GAAGTAAATAATTTGTTTTTACTTTTACAGCCTCATAGGTGGAAGGAAGT  
TGACTTGAATTTTACAGATGAGACTTTGGACTTTGGGACTTTTGGGTTGGGG  
CTGGAATGAGTTAAAAGTTGGGGGGATTATTGGGAAGGCACGATTTTATT  
TTGCAATATGAGAAGCACATGAGATTGGGGGACCAAGGGTGAATAATA  
TGGTTTGGATGTTTGGCCCCCTCCAAATCTCACATTGAAATGTAATCCCA  
GTGTTGAAGTGAGGCTGCTGGAAAATGTTTGGATTACAAGGCTGTCTGAG  
CACATTGGATAAGACGTGTAGGNCCC

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CGCAGCTCGCTGGTTAATTCTGTGGCTCCTGTGACCCTATTATAGCACC  
AGGTCTATGACCAGGAGAATTAGACTGGCATTAAATCAGAATAAGAGATT  
TTGCACCTGCAATAGACCTTATGACACCTAACCAACCCCATTTTACAA  
TTAAACAGCAACAGAGGGAATACTTTATCCAACCTCACACAAGCTGCTTTC  
CTCCAGATGCTGCTTTTGGCTTTATTATTTTATAGAGATGGGGGCT  
TCACTATGTTGCCACACTGGACTAAAACCTCTGGGCCTCAAGTGATTGTC  
CTGCCCTCAGCCTCCTGAATAGCTGGGACTACAGGGGCATGCCATCACACC  
TAGTTCATTCTCTATTTAAAATATACATGGCTTAAACTCCAAGTGGGA  
ACCCAAAACATTCATTTGCTAAGAGTCTGGTGTCTTACCACCTGAAGTAG  
GCTGGCCACAGGAATTATAAAAGCTGAGAAATCTTTAATAATAGTAACC  
AGGCAACACCATTTGAAGGCTCATATGTAAAATCCATGCCTTCTTTCTC  
CCAATCTCCATTCCCAAACCTTAGCCACTGGCTTCTGGCTGAGGCCTTAGC  
CATACCTCCCGGGGCTTGACACACCTTCTTCTACAGAAGACACACCTTG  
GGCATATCTTACAGAAGACCAGGCTTCTCTCTGGTCTTGGTAGAGGGCT  
ACTTTACTTTAAACAGGGCCAGGGTGGAGAATTCTCTCCTGAAGCTCCATC  
CCCTCTATAGGAAATGTGTTGACAATATTGAGAAGAGTAGGAGGATCAAG  
ACTTCTTTGTGCTCAAATACCACTGTTCTCTTCTTACCCTGCCCTAACC  
AGGAGCTTGTCAACCCCAAACCTCTGAGGTGATTTATGCCTTAATCAAGCAA  
ACTTCCCTCTTACAGAAAAGATGGCTCATTTTCCCTCAAAAGTTGCCAGGA  
GCTGCCAAGTATTCTGCCAATTCACCTGGAGCACAAATCAACAAATTCAG  
CCAGAACACAACCTACAGCTACTATTAGAATATTATTATTAATAAATTC  
TCTCCAAATCTAGCCCCCTTGACTTCGGATTTACGATTTCTCCCTTCTC  
CTAGAAACTTGATAAGTTTCCCGCGCTTCCCTTTTCTAAGACTACATGT  
TTGTCTATCTATAAAGCAAAGGGGTGAATAAATGAACCAAAATCAATAACT  
TCTGGAATATCTGCAACAACAATAATATCAGCTATGCCATCTTCACTA  
TTTTAGCCAGTATCGAGTTGAATGAACATAGAAAAATACAAAACCTGAATT  
CTTCCCTGTAAATTTCCCGTTTTGACGACGCACTGTAGCCACGTAGCCA  
CGCCTACTTTAAGACAATTACAAAAGGCGAAGAAGACTGACTCAGGCTTAA  
GCTGCCAGCCAGAGAGGGAGTCATTTTATTGGCGTTTGTGAGTCAAGCAAGG  
TATTGTCTTACATCTCTGGCTATTAAAGTATTTTCTGTTGTTGTTTTTC  
TCTTTGGCTGTTTCTCTCACATTGCCTTCTCTAAAGCTACAGCCTCTCC  
TTTCTTTCTTGTCCCTCCCTGGTTTGGTATGTGACCTAGAATTACAGTC  
AGATTTCAAGAAATGATTCTCTCATTTTGTCTGATAAGGACTGATTGTTTT  
TACTGAGGGACGGCAGAACTAGTTTCTATGAGGGCATGGGTGAATACAA  
CTGAGGCTTCTCATGGGAGGGAATCTCTACTATCCAAATATTAGGAGA  
AAATTGAAAATTTCCAACCTCTGTCTCTCTTACCTCTGTGTAAGGCAAA

FIG. 3 (26 of 52)

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TACCTTATCTCTGTGGTGTTTGTGTAACCTCTTCAAACCTTTCATTGATTG  
AATGCTTCTTCTGGCAATACATTAGGTTGGGCACATAAGGAATACCAACA  
TAAATAAAACATTCTAAAAGAAGTTTACGATCTAATAAAGGAGACAGGTA  
CATAGCAAACCTAATTCAAAGGAGCTAGAAGATGGAGAAAATGCTGAATGT  
GGACTAAGTCATTCAACAAAGTTTTCAGGAAGCACAAGAGGAGGGGCTC  
CCTCAGAGATATCTGGATTAGAGGCTGGCTGAGCTGATGGTGGCTGGTG  
TCTCTGTGTGCAAAAGTCAAGATGGCCAAAGTTCCAGACATGTTTGAAGA  
CCTGAAGAACTGTTACAGGTAAGGAATAAGATTTATCTCTTGTGATTAA  
TGAGGGTTTCAAGGCTCACCAAAATCCAGCTAGGCATAACAGTGGCCAGC  
ATGGGGGCGAGGCCGGCAGAGGTTGTAAAGATGTGTACTAGTCCTGAAGTC  
AGAGCAGGTTCCAGAGAAGACCCAGAAAACTAAGCATTCCAGCATGTTAAA  
CTGAGATTACATTGGCAGGGAGACCGCCATTTTAGAAAAATTATTTTGA  
GGTCTGCTGAGCCCTACATGAATATCAGCATCACTTAGACACAGCCTCT  
GTTGAGATCAGATGCCCTGATATAAGAATGGGTTTTACTGGTCCATTCTC  
AGGAAAACTTGATCTCATTCCAGGAACAGGAAATGGCTCCACAGCAAGCTG  
GGCATGTGAACTCACATATGCAGGCAAATCTCACTCAGATGFAGAAGAAA  
GGTAAATGAACACAAAGATAAAATTACGGAACATATTAACTAACATGAT  
GTTTCCATTATCTGTAGTAAATACTAACACAACTAGGCTGTCAAAATTT  
TGCTTGATATTTTACTAAGTATAAATTATGAAATCTGTTTTAGTGAATA  
CATGAAAGTAATGTGTAACATATAATCTATTTGGTTAAAAATAAAAGGAA  
GTGCTTCAAAACCTTCTTTTCTTAAAGGAGCTTAACATTCTTCCCTGA  
ACTTCAATTAAAGCTCTTCAATTTGTTAGCCAACTTCAATTTTACAGAT  
AAAGCACAGGTAAAGCTCAAAGCCTGTCTTGATGACTACTAATTCAGAT  
TAGTAAGATATGAATTACTCTACCTATGTGTATGTGTAGAAGTCCCTAAA  
TTTCAAAGATGACAGTAATGGCCATGTGTATGTGTGTGACCCACAACAT  
CATGGTCATTAAAGTACATTGGCCAGAGACCACACTGAAATAACAACAAT  
TACATTCTCATCATCTTATTTTGACAGTGAAATGAAGAAGACAGTTCCT  
CCATTGATCATCTCTCTGAATCAGGTAAGCAAATGACTGTAATTCTCA  
TGGGACTGCTATTCTTACACAGTGGTTTTCTTCATCCAAAGAGAACAGCAA  
TGACTTGAATCTTAAATACTTTTGTGTTTTACCTCACTAGAGGTCCAGAGA  
CCTGTCTTTTATTATAAGTGAGACCAGCTGCCTCTCTAAACTAATAGTTG  
ATGTGCATTGGCTTCTCCAGAACAGAGCAGAACTATCCCAAATCCCTGA  
GAACTGGAGTCTCCTGGGGCAGGCTTCATCAGGATGTAGTTATGCCATC  
CTGAGAAAGGCCCCGAGGCCGCTTCACCAGGTGTCTGTCTCCTAATGTG  
ATGTGTTGTGTTGTCTTCTCTGACACCAGCATCAGAGGTTAGAGAAAGT  
CTCCAAACATGAAGCTGAGAGAGAGGAAGCAAGCCAGTTGAAAGTGAGAA  
GTCTACAGCCACTCATCAATCTGTGTTATTGTGTTTGGAGACCACAAATA  
BACACTATAAGTACTGCCTAGTATGTCTTCAGTACTGGCTTTAAAGCTG  
TCCCCAAAGGAGTATTTCTAAAATATTTTGAGCATTGTTAAGCAGATTTT  
TAACCTCCTGAGAGGGAATAATTGGAAAGCTACCACTCACTACAATCAT  
TGTTAACCTATTTAGTTACAACATCTCATTTTGTAGCATGCAATAAATG  
AAAAATCTTCTTAAAAAATCATCTTTTTATCCTGGAAGGAGGAAGGAAG  
GTGAGACAAAAGGGAGAGAGGGAGGGAGCCCTAATGAAACACCAGTTACC  
TAAGACCAGAATGGAGATCTTCTCACTACCTCTGTTGAATACAGCACCT  
ACTGAAAGAACTTTTATTCCCTGACCATGAACAGCCTCTCAGCTTCTGTT  
TTCCTTCTCACAGAAATCCTTCTATCATGTAAGNTATGGCCCACTCCAT  
GAAGGCTGCATGGATCAATCTGTGTCTCTGAGTATCTCTGAAACCTCTAA  
AACATCCAAGCTTACCTTCAAGGAGAGCATGGTGGTAGTAGCAACCAACG  
GGAAGGTTCTGAAGAAGAGACGGTTGAGTTAAGCCAATCCATCACTGAT  
GATGACCTGGAGGCCATCGCCAATGACTCAGAGGAAGGTAAGGGTCAAG  
CACAATAATATCTTTTCTTTTACAGTTTAAAGCAAGTAGGACAGTAGAAT  
TTAGGGGAAAATTAACCGTGGAGTCAGAATAACAAGAAGACAACCAAGCA  
TTAGTCTGGTAACATACAGAGGAAAATTAATTTTATCCTTCTCCAGGA  
GGGAGAAATGAGCAGTGGCCTGAATCGAGAATACTTGCTCACAGCCATTA  
TTTCTTAGCCATATTGTAAAGGTCGTGTGACTTTTAGCCTTTTCAAGAGAA  
AGCAGTAATAAGACCATTACGAGCTATGTTTCTCTACTAATACTATGC  
CTCCTTGGTCATGTTACATAATCTTTTGTGATTGAGTTTCTCTACTGT  
AAAATGGAGATAATCAGAATCCCCACTCATTGGATTGTTGTAAAGATTA  
AGAGTCTCAGGCTTTACAGACTGAGCTAGCTGGGCCCTCTGACTGTTAT  
AAAGATTAAATGAGTCAACATCCCCTAACCTCTGAGTGAATAATGTCT

FIG. 3 (27 of 52)

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GGTACAAAGTAAGCACC AATAAATGTTAGCTATTACTATCATTATTAA  
ATTATTTTATTTTTTTTTTTTGGAGATGGAGTCTCACTCTGTTGCCCAGGC  
TGGAGTGCAGTGGCGCAATCTTGGCTCACTGCAAGCTCTGCCTCCTGGGT  
TCAGGCCATTTTCTGCTCAGCCTCCCGAGTAGCTGGGACAACAGGCAT  
GTGCCACCATGCCAGCTAATTTTTTTGTATTTTAGTAGAGATGGGGTT  
TCACTGTGTTAGCCAGGATGGTCTCTATTTCTGATCTCATGATCCGCCT  
GCCTTSGCCTCCCAAAGTGCTGGGATTACAGGCGTGAGCCACCGCGCCCG  
GCTATTATTATTATTACTACTACTACTACTACCTATATGAATACTACCA  
GCAATACTAATTTATTAATGACTGGATTATGTCTAAACCTCACAAGAATC  
CTACCTTCTCATTTTACATAAAAGGAACTAAGCTCATTGAGATAGGTAA  
ACTGCCCAATGGCATAACATCTGTAAGTGGGAGAGCCTCAAATCTAATTCA  
GTTCTACCTGAGTAAAAAATCATGGTTTTCTCCTCCATCCCTTTACTGTA  
CAAGCCTCCACATGAACATAAAACCAATATTCCTGTTTTTAAGATAATA  
CCTAAGCAATAACGCATGTTTACCTAGAAGGTTTTAAATGTAACACAAT  
ATAAGAAAAATAAATCACTCATATCGTCAGTGAGAGTTTACTACTGCCA  
GCCTATGGTATGTTTCTTAAATCTTTGCTATACACATACTACATGT  
GAACAAATATGTCTAACATCAAGACCACACTATTTACAACCTTATATCCA  
GCTTTTCTGACTTAGCAATGTATTGATGACATTATGCATGCTTAGACCTC  
C

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GTATTCTATTCTCGGTTATAACACAATCACAGTGATTGTGCATATCTTTC  
CAGGATTTGTTAATTTCACTTCTTCAGCTGTTTCCCCCTGTTGGCTGGA  
ACTGATTTTCTATCTTCTGGGAGAATCTTCAGCAAGCCAACTCAGGATTT  
GTTGGGTGCATTTTGTCAAGTCTAGGACCCAGGCTCTGGGTGACTGATTT  
CCTCTAATTACCGAGCAATGTAAATGAGGAAGTCTGATTGTGTAAAGGT  
GTTAAACTTTTGTGTGACGGCAAACTTTAATACCATGAATAGAGATTCC  
AGAATTTTCCAACCTTCTAACGGGATTCCTTTCACTCCCTGACATTAGAAT  
GTTAGAAAACTACCACAAAACATCTGTGAGGCTATCCTACAAGGCCCGT  
TTTTCAAAATAGGTTTTTACAAGGATTGCTATTTGGGATGATAGTTTCAG  
AAAGGCGCTATCAAAGTTAATTGATGATGTGTGCAAGCTGAAAGTTATAT  
GTTAGAACTAGCAGTATTTCAAAAATATCCCTTTTAGGCTTTTTTGCTAA  
TATATCTGCTCATTTTCAAAGTTCCCAATATTATAAACTTTTTAAAGCA  
GAAAGAAGAACCCTCCATTTCTGCTGGCCCCCTTCCCTGTTCAACTAAAAA  
GTATTTTCCCAGGCAATGCTATCCCAGGACTCACACTCCATCCATCCATC  
ACCTACCATAAGTTCTTTGAAGGGCTCATTCTGAGCGCTTCTCTGAGTGCC  
TGGGATCTGTTATTTCTCTCCATTTCTGCTGCTGCATGGTAGTCCAAGTC  
CTCCTCCCTTTTCCCTAGGCCATTTGAATCATCTGCTAATTGGTTTTCC  
TGATTCCCACGGAACTTCTCCATCCCTTCTCACATATCAGCCACAGA  
AGTATCTCCAAAAGCAAATCTGGTGACATGAAGCCCTTGACAAAACCC  
ATTCATTACTGGTTCCACACCTCCTTTGTGGATAAGTTCAAGCTCCTGAG  
TGTGGCAAGCAGGGCCACCTGGAATCCCTGCCCCCTCTCTCTATCCCA  
CGCATCAATCTTCTGTCTATTTGCAGTTCCTTGAATGTGATATCTTT  
CTAGTCTCTGTGCTTTTGCTAACCTGTTCTTCTGACTGGAACTCCTT  
CTCCTCCTTGTAGTTTGGCTAATTTCTAGTCTTCAAGACTCAGCTCATG  
CTTCAGCCCCCTCTATAACAAGTCCTTTCCCAAGCTGGGTGGTGGATGCTC  
CTCTGTGCTGTGTGAGTCTTGAACATCCTCAGCAAACCTCAGCTTTGTTT  
GCTTGTCTCCCTTGCTGTCAATGCACCTGATTGAGGCTGGCATATACTG  
TTCACCTCCATGACTGGCTCATGGTGGTGTCCGTGAATATCATCCACCC  
AAACGGATGAGAGCTACCATGCCATCACTTGTGACTTCCATCTGGAGCTA  
ACCTCCCCGACAGGAAAGCGTTTCCCTTAGGAAAGAATATCTTTGGGTTA  
AATAGAAGTAGAGACTCACCAGAAGCACTATGTCCAGCTCAGAATGAACT  
GCTCAGTAAGCAGCCTTGTCAATGAGGAGGAGCAGGCCAGCCCCAGAGG  
CCTCAAAGTGGGAGAGTAGAGAAGCGCAGTTCTGCCACAAAGGCACAGT  
GGACACCTTGCTCCCTGGCTGGCTGGAAGCAGATGGTGTCCACCTGCTT  
CCATGGGAATTCTGCACCTTTAATAAAGTTTTATGGGACAGGAAGGTGAC  
TGGCATTGACATTGTAACGAGGAATGGGTGGTGCCACCTTTGCTGTGTCT  
TACCAGAAATACCTGTGGCAGGTAAATTTCTAGAGAGACCCTCCCATTTC  
TCCCATATAGCAATTTTGAATGTTTCTGAGGGCTTTCAAATTCATCT  
GGGAACATAGGAGTTCCAGAAAGATGAAATCAAAGGTGATGGTATGCCAA  
AGAAAGTAGCTTTTAGAATGACTTACATTAGCCATTTCATCCATTGAGCAC

FIG. 3 (28 of 52)

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ACCAGGCATTGAGTTTGAGGGGTGTGTGTGTGTGTGCGCGCGCGCGCG  
 CGTGCATGAGTGCATGCGCGCGCGGTGTACATAGGGGAAGGAAAAA  
 AAAAGTACACAAGACATGATAGTTGTCTCAAGGAGTTTTTGCAATGTT  
 CACAATTTAAGAGAAATATGCTGTGCTGTGGCTGGTGTATAAACCAACTGC  
 TAGGGAGAGGCCCTCCACACACACTTGGGGGCAAAATGCGACCTCTAGGACT  
 GCCAGTGGAACTCTGGGCATGCTGTTTGTGGTGCATAAACCCCTGGTCCCTT  
 GATCAGGGACCTATGTTTACTTTCTCTCCCTGGAAGTCTTCATTAGTG  
 GGCATCCAGAAGGTCTTGCAACAGGCGAGGGAGGCACAAAGACAAGAGT  
 TTGAAACCAGCCTGGACAACAAAAATGAGTTTCTATCTTTACAAAAAAAT  
 TTTTAAAAAATTAGCCAGGTAGGATTGCATGTGCCTGTAGTCCCAGCTAT  
 TCAGGAAGCTGAGGCGAGGAGGATTCCCTGAGACCAGGAATTTTGAGGCTG  
 CAGTGAGCTATTAAAGTTGGCGCAAAAGTAATCGTGGTTTTTATCATTAAA  
 AGTAATGGCAAACTTTTAATGACAAAAACCGTGATTACTTTTGACACAA  
 TTTAATATGATTGACGAGTGCAGTGTGCTCCAGCCTGGGCAACAGAGTG  
 GGACCCTGTCAAAAAATAATAATAATAATAATAATAATAATAATAATAA  
 ACCCAAAAAACAAAAAAATGGGTGTGAGACCCCTGAATTGAGGAATAA  
 TAGGAAGGAGTGTGATTCTGTGTGTGCATGCATGGGTGTGCACCTCAGT  
 GCCTGGGTGGCTTACCCTGGGCTAGTTCAAGGTGGCAATGGTTTTCTCTC  
 AGCTGGGCTACCACTCTTCCCCAGGGCCTGTCCATGTATTTGGTGGC  
 AAGATACCTATGGACTAGAGTCCCTCCTCAGAGGAAAGGCTCCTCCCATT  
 TCTCTGGCTTTCAGGTAGTAGTCCATGACTTCAACAGGTCCCCAGTGCAA  
 TGTATGGGTTAGTTTAGTGGGTCTCCTCTGAGAGCCTCCCATAGCCC  
 AAAAGGCCCTGTCTAGCTGGCAGTCATCTCCTCTCTCCAGCTCTCAG  
 CCTTCTCTTTGCTCATCCCACTCCGCAACAGGCTTTCTGCCTGATCCTTG  
 GATGTGTCAATCCTGCCCTAAGGGATGCAAGGCAATTTGTCTTTTATT  
 ATTAAGATCTCTCTGAGGCCACGTGTGGTGGCTCACACCTGTAGTCTTA  
 GAACTTTGGTAGGCCAAGGTAGGAGAATTGCTTGAGCTCAGGAGTTCAG  
 GCTGTAGTGAACCATGATTGCACCATTGCAATTCAGCCTGTGTGACACAG  
 CGAGACCTGTCTTTTCTTTTTTTTTTGAGACAGGGTCTCGCTCTGT  
 CATCCAGGCTAGAGTGCAGCGGTGTTTTCTGCTCACTGCAGCCTCAACC  
 TGCACATTTTTTGTAGAGACGGTGTCTTGCTATGTTGCCAGAGTGGCCT  
 CAAACTCCTGGGCTCAAGAGATCTTTCACCTCAGCCTTCAAAGTGCTG  
 GGACTACAGGCGTGAGCTACCGCGCCCAACAAAGACCCTGTCTTAAAAAG  
 AAAACAAAAATAAACAACTCCCTCAAGTCTTTTTTTTTTTTTTGAGACGG  
 AGTCTCGCTCTGTGCGCCAGGCTGGAGGGCAGTGGCGCAATCTTGGCTCA  
 CTGCAAGCTTGCCTCCGGGTTCAGGCCATTCTCTTGCTCAGCCTCCC  
 GAGTAGCTGGGACTACAGGTGCCCCGCCACACCGCTGGCTAATATTTGT  
 ATTTTGTAGTAGAGATGGGGTTTCACTGCGTTAGCCAGGATGGTCTTGAT  
 TCTCACCTTGTGATCCGCGCGCTCGGCCTCCCAAAGTGCTGGGATTAC  
 AGGCATGAGCCACCGCGCCAGCCAGACCTCTTGAGTCTTAAACTCCTCT  
 GTAGTTCCAGCCACCTTTAGCACATGACTCTGTTAATTTTGTCTCACT  
 CTCTGAAATCATCTCTGTCCACTCTTGACTGACAGGTCTCTGCACTAGC  
 CCACTGCTTAATCAGATAGGTCCCTGTCAACTATTCAATATTGTGTCCC  
 CATGCCAGTGTGGATGATTAATAATTTGAGTGGAGGCTGATCAGATGAG  
 CCATCTCCTTCCAAGTCTCACTTGCTGGCTCCTGCTTAGTTTATGCTC  
 CCACTCTTCAAAGAACGTGAGCCCTGGAAAGTATTTTAGTCATTTAGTTC  
 AGTGCTTTGGATGGGAGGATCACATCCCTGGGTCCCGTCTGCAGACTG  
 TTTTGCTCTAGCTGACTAGGCAGGATTCCCTGCCTTCTCTCACTTCGGCA  
 TGGGACTTCTTCTGAAATGTCTGCTCAGTCAAGAGAATGACCTTCCCCA  
 AGCAATCTTACTCCACAGGCACTAAAGGTGTGTGAGAGATCTCTGTCT  
 CATCTTTCTGGCCAGGTGCCAACGTGAGTTTATAGCCAAGGGACAAGACT  
 AGTTAGCAGATCAGGCAGGTCTTAGACCCAGCGTAAGTGCCAGACTTCT  
 AGCTGCAGTTGTTCTGCCCCACTGGGCGTTCAAGTGGAGAGAGGGCAT  
 GGCACTACACTGAGCTCTCGGCGAAACCCAGGACTCTGAAATCTCGGTGT  
 CAGCCAAGGCCACTCTTTTCAGCAGGACTTCAGTCAGTCCTGTCACTAG  
 GCTGTCGAGCACATGGTAGGCTTTACCCC  
 >Contig35  
 AAGGAGTGTGCTTGTGCTGATAGCATGTGTGANGGGACGAGGAGTAAATAAT  
 TTCTGCCTTCAAGAAATTGCAAACTAGTAATGGAGATAAAATCAACAGAG  
 GAACAAATTAGAGTATAAGGTAAATCTAAGGGCCATAAGAGAGGAGAGA

FIG. 3 (29 of 52)

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AGTATGGGAGTTTCAGAGGAGGGGGTAAATGAGGGGAGTAGGTGGGTAGA  
AAAGGTTAAAGTAAATAATGATGGGAAGGAAGACAAAAGACGACAGGG  
GTGCCAAAGGACTCTTAACCTCATCTGAACGGAGTTGCCCTGTTTTGCTC  
TCTGATGCTCATGTATCTATCCTTAGAGACAGCTTGGCGGGCAATGTAGA  
GCGTAGGGGCTGACATAGGGGGTTGGAGTCCACCTCCGTGACTTCTAGC  
AAATTAGCAAACCTTTGCTGCTGCTAAGCCTATAAGGCGGACAGAAATGCC  
ATCTTTAAAGCTTGTTATGTAAAGTGCCTAGGACCTCGTAGGCATCAACA  
GGAATAATGGATGAAACAAAACAACGGTGCCTATCTTGGAGAAAGTGGCA  
TCTGAGCAGGAGTATTTTGAAGGTAGGAAAGGGCTCCAAGCACATCTAA  
GAGATTAGGGAACGACAGCCTTAGCCCTGGGTGCAGATTTAACCAATC  
AACTTCTAACACCGCAGGCTGAGAGGTGTGGAGTGAGAGCCCCGCCAGA  
GGCAGGAGACCCGGGCTTCGGCCAGACCCCGCTCCTGGTACAGAGGACC  
ACGCCCCGGCTCTGCCTGGAGCCAAATGTGGATCAAAACAGCGCGCAGCTT  
CCCCTGCTGGTGAACACCCGAGCAAGGGGCTCAGTTTCTTTATCCGGA  
ACGTGGTGACAATGACATCTCTTTGCAAGGCTGCTGCAGGGCTTTCTGGA  
AATACGCCCCGTGAGGTATCTGGGCTGCGCACAGCCTCCCCCGCCAGGA  
CCCAGACGCTACCTGGGGTCCCGTCTGCGCTCCCGGATGGAACACGC  
CCAGGGGAAACTTAGCGAGCGGACGGGACCTCCCGCGGGACGAA  
CTCACTCGGTGGCTCCTACTTCCCCGGCGGTGTCCAACGCCTGAGAAT  
AACGGGAACAGCGGTGCTACTCACCAGCAGCGGCAGCAGCGGTAGGCCCG  
GGCCCCACCATGACTCTTCAGTGACAGTTTTTCTTCAAACGCGCSCCTG  
TAGCCAGGACCGCGCTGCCGCGCTCCACGCGTCTCATTGGCTCCTGCG  
GGTTTGAAACTCGCTAGTCGTGACACGGGAGGGCGGGACAACAGGCAAT  
AGGCTCTTTGCGGTGGCTCTGGCCTTGAGAACCCGACCTTGGGGCCCTT  
TGATTGGAAGAACGTGACGCGACCTCGGCATTGAGGGCGGCTTCTCGG  
GGCGCGGGCGCGCCGCTCTGAGTGCCTGTGAGTGCCTCCGAGTG  
GGCGTGGGACCTCCGTGGGGGCTCAGCCGGGCTGGTGGTTGGGGGGCG  
GTTACGCTGAATCCAGCTGGGGTTGGCGCGCGGGAGTCCCTGGGCGGAG  
AGACAGGGCGGTCTCCAGGATGCTGGGGCGCTACCTGATTCTGTCTT  
TTCAAAGTCTCAGACTCACAGGAGCTGTAAAAAATAATATTATAAAGAG  
GACATATGGGTCTTATGCATCTAAAGGCTCCTAGTTCTTAGTACTGCAGG  
GTGGCTCGTTTAAATGTGGTAAATATGCATAACATCACATATAACATTT  
TAACCATTTTAAAGTGTAAATTTTCAAATGTGCAGTTTAGTGGTAT  
TAAGTACCCTCACATTGTGGCACAGCCACCACTACTGTCTTTCCAGAAC  
TTTTTCATCTTCCCAAATGAAACCTGTACCCGTCACTAACTCCGCACTC  
CTCCCTCCCCCAGCCCCAGGCAATCACCATTCTAGTTTCTGTCTCTATGG  
ATTTGACAACGTAGGTGCCATATAAGTAGAATCATGCAGTATTTGTTCT  
GTGACTGGCTTGTTCACCTAGCATAAAGTATTCAAGGTTCAATCATGTG  
TAGCATGTGTGAGAAATTCCTTCTTTTAAAGGGGAATAGCATTTCTGT  
GTGTGGAGATGCCACATTTGCTTCTTGGTCCATCCCTCTCCGGACACTT  
GAGTTGCTTCCACTTTTGGCTATTGTGAATAATAATGAACATGAATG  
CACAAATAACTCTTTGAGACTCTCTTTTCACTTTTGGGTATATACCA  
CGAAGTGGTATTGTTGGATCAAACGGCAATCTATTTTAAATTTTTGAG  
AAACTGCCCTACTCCTCTCACGGTGATCTCTTGTCAAGGTATATTTTCG  
ATTTACCTGATCAGCTGACTATAAGGCCATAAGGCTAACGGAGAAACGC  
AGGCCTAGTTTCTCCTAGTTACTAGGAGATCGCAGGCCTCGTTGTCTGA  
ATCCCTAGACACACTTCATTCCCCTTGTTTTAAATCCTAAATTTTTTTCT  
TTTGAAGTTTGTCTGTTTCACTATTCTCCAGTTTCTTAAAGAGGTCTG  
GAAAAATGCTTTTGGCTCCTTGTGTATGAAGGTTCTCTTCCATGGATGCT  
GGAGAAGTCGTGTGTGGAGGGGAGTCATATCTGGGCACCTGTTGGCCAG  
GTTAGCTTACCAGTTGGGTACTCAGCAGGGCATGAAGCCACTGCAGCAG  
CCCTTCTCTTTAGCCGTAATAGGGAGTTTGAAGAGAGCCAGGGTTTCT  
GGATTTATGCATTTTGATATTTTCAATAGTGTATTAATGTTTAAATAG  
GAAACTGATCATTATTTTGTAAATGACTGAGAAAGGACTCCTTACC  
AACAGTTTTCAGAAAAGTGAAGGCGGTTTTGTTTTGGTCTTTGTAGAATCT  
AGGTGGTTGAATGCATGTGAGTTGTAGAAGTCACCTTGCTGATATCCCA  
CGCAGTGCTGGAGTATTCACAGACCCCATGTAGGTACTGCACCTTTGCA  
GGTATACTGCTGGTGTGGTGGAGCTGCCTTACCTGTCTGTTATTGGAGA  
CCCCTGCTTATTAGGAACTTAAATGAACTCAAATGAGCTTCTTGCTT  
ACTGGTCTAGTCTTTTGGAGCAACATAGGCCAGTTCTGCCTCGTTTTTT

FIG. 3 (30 of 52)

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TCCATCCTTTGGGTATTTGACGGTCTATTTTGTAGGACACAAAATGTGGG  
AAAAATAGCTAGGCAGGTTTAAAAATTTCTCAACTCTACCAAGCATGGTGGC  
TTATGTTCTTAATCAATCCCAGCACTTTGTGAAGCTGAGGCAAGAGGATT  
GCTTGAGCCTAGGAGTTTGAGACCAGACTGGGCAACATAGCAAGACCTCG  
TTTCTTAAAAAATAAATAAATTACAAAAATTAACCAGGCATGGTGGCA  
CACACCTGTAGTCCCTTCTACTCAGGAGGCTGAGGTGGGAGGATCACTTG  
AGCCCAAAAGTTGAAGGATGCACTGCACTGTGGTTCATGCCACCAGCACTCC  
AGCATGGGAGGCAGAGCAAGACCCTGTCTCCAAATAAATACATAAATTAA  
ATTCTTAACCTCATTTCATCAAGTATCCACTGTAGCTTTCCATCATCCTGG  
TGTTGTTTTTTTAGAAGGATCTGGGTCCATTGCCGGCTAGAGTGCAGT  
GGCATGATCTCAGCTCACTGCAGCCCCCACCCTCTCTGGCTTAAGCGATCA  
CCCACTTCAGTCACCCATCTGGGTAAATTTTGTATTTTTGTAGAGATGG  
GGTTTTGCCATGTTGCCCCAGGTGGTCTTGAACCTCTGGCTCAAGCGAT  
CCATCTGCCTCCATCTCTAAAGTGTGGGATTACAGGTGTGAGCCACCA  
CACCAGGACAATCCTGGTGGCTTTTAACGGTTTTCCATTGCTCTCAGGCT  
AATGACCTATAAGCCCCCTGCGGGCTTGGCTTTTACTCCCTGAGCATTAG  
CCACCTCCCTTAGCCTTAGCCCACTACTCTCCCTTGCTCAGTGTTAT  
CCAGACACTTTGTTTTTCTTTCCATACTCTCTCTGTCTGGGAATCCA  
ACCTTTCTTTCTCATTCTCTAGTTGATTATTATTATTTTACTCTAGCA  
GCCTTATTGAGATATTTACATACCGTACGATTCTCCCACTTACAGTGTAC  
AATTCAATTTTCTAACATTTTCATCACCCTTAAAGAAACCTATACTCA  
TTAGCAGTCACTCCCCATTCTCCCCCTCTCTCAGCCCTAGAAACCATGA  
ATCTACTATCCATCTCTATAGATTGCTCTCTGGACATTTTCATATGTATG  
AAATTATGCAATTTGTGGTCTCTGATGGGCTTCTTTTGTACCAAAATAT  
CATGGGTTTGATCTAGGTCTCTGCTGCTCGCTGCACAGAAAGCCAGCCACT  
GAGATGACAAGTATTGCCAAGGAAGAAGGCTTTAGTCAGGTGCTGCAGCT  
GAGGAGATGGGGCTCAATCTCAAATCCATCTCGCTGACCTAAAACAGG  
GGTTTGGATAGCAGGGAAGAAATGTAACAATGCGTAAGAAAACAGGAACC  
AGGGAGGGGCAAGGAAGCAATCCTGATGAATGAGTGGTCCAAAGTCTCAT  
TGCCTGGATGTGGTATCTGGCGAGTTTCAGTTCTTTGATACTTTTTTTG  
AGAGGCCTGAAGTCTTTTCCCCAGGAAGGAAGTCAAAACAAAACAAATACA  
AGCTTCCAGCTTTAAGACCAGAAGCGTCAATTTCTATGTTTATCCGAAAG  
AACAGTCTATGGGACTATTGGTTAAGTTTCACTTTCACTTAGTATGCTGT  
TTTCAAGGTTTATCCACATAGCATGTGTGAGTACTTCATTCTTTTATGAC  
TGGGTATTCTATTGTGCGGATATACAATATTTTATTTGCCATTTCATCAGT  
TGATGGACATCTAGGTTCTTTCCACTTTTGGCTATTATGAATAATGCTG  
TTATGAACCTTTTCATGTATAAGTTTTTGTGTAGACATATGTTTTCAACACT  
CATGGGTATATAGCTTTTATGAGAGGAATTACTGTGTATACGATAATTCTA  
TCTTTAACCATTGAGGAAGTCCAGACTGTTTTCCAAAGCAGCTGCAGC  
ATTTTACATTCTTACCAGCAGTGTATGAAAGTTCCAGTTCTTTTACATCC  
TCAACAACACTTGTATTGTCCATCTTTTAAATTACAACCATCCTAGTGG  
TTGTGAAATGGTATCATTGTGGTTTTTATTTGTATTTCTTGATGACT  
AATGATGTTAAGCATCTTTTTATGTGTTTACTGGCCATTTGTATATCTCT  
ATTTCAGAGTCTTTGCCAATTTTTAAATTGGGTGAGTTGTCTTCTTCTTT  
TTTTTTGAGATGGAGCCTCACTCTGTTTCCAGCTGGAATACAGTGGTGT  
GATCTCAGCTCACTGCAACTTCCACCTCTGTGTTCAAGTGATTCTGGTG  
CCTCAGCCTCCCAAGTAGCTGGGATTACACGCACCTGCCACCATTCCAG  
CTAATTTTTTTCTTTGTATTTTGTAGTAGAGACGGGGTTTACCATGTTGG  
CCAGGCTAGTCTCTTTGTTGACTCTTAACCATCCTTCAGTCTCAGACAAA  
ACATCCCTTTCTCAAGGATTGTGATTAGCTTGATTATTTGCTTATCTTTC  
TCCCTGCTAGTCTGTAACTGAGGGTAGGCCACTATATTCAATTGTTCTTG  
GCACCAAAATAGAACTAAATTAATGTCTTTTGAATGAATAGGGCTTTCTC  
CTTTTAAAGATCCCTTCAATACAGTAACCACACTATATATAAGTAGCCAC  
AAGCCCATTCATAATACTACTAGTNCCTTGCGCCAAACC  
>Contig36  
GGCTCAGCGTTACTATACTGGTCTCAAACCTCCTGGGCTCAAGCGATCTGC  
CCCCCTCGGCTTCCCAAAGTGTGGGATTATAGGCGTGAGCCACGGTGCC  
TGGCCTCAAATAACTATTTAAGTGAACAAAACCTAGTATGGCACTAATGA  
AAAATGTATAAATCCATAATCGCAGAGGGATTTCAACTTACTTCTTTCGA  
TTATGTAAAGGTCAAACAGACAAAAGACAATGACAAAACCTTAATGCAATG

FIG. 3 (31 of 52)

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AACACTTTTGAATTAATGAACATATATTGGATATGTACCCAAGAATTAGA  
GAATACATACTAGTTTTGAGTTTATGCAGAACATTTACAAAAATTTAGTG  
GAAGCCTAAATTATAAAAAAGTTGCTGTCACGTAGAATAACACACAAACCC  
CTGAGTCCGGAATTCAAAGCCCTCCACACTCTCCTCTACCTTTGCATCTT  
TATCCTCCACCACTGTCAGTGCATACTCTGGGCTACTACTCACTGTTCT  
TGATTCAAATTCATGTTCTGTCAGCTCAAATCATTCTCTGCTGCTGGAA  
TACTACTTTCATACATATTCTGCTATTGAATTCTTGTCTTAGCACCCCAT  
CTACTCCAAGACGATGTCCAGTTGGGGTTACTCCCTGTCCCATTTTCTTT  
GATTACACTTTTTTTTTTCTACTTCCATTATATTATTGATCACATCTGTGC  
CACAGTTTTTGACTTTGTGTCTGCTTTTACTCTTTTCTAGACCCTGATAG  
CTCCTGAAGGGTTGGGTCATTTCTTTTTTATTTGCTCATTCTCATGGCA  
CAGTGAGTGCTTAATAAATGGCTATTGACTGAAATTAAGTGTATCTAAA  
TGGACATATTCCACTTCTGGGCCATTCTTTCTTTCTATTGGAACCA  
GGAGATGGGGAACCATAACAAAGGTAAGGTTGTCCATGTGAAAGAACAT  
GGAACCTTCCCCTGAGGGCCAAAAAGAGCAGGGAAAGGTGCAAGACAA  
AATCTTCCATTTTTTAAACAATGTAAGAATGTGGTCCACCTCATGCTCAGG  
TGGGACTTTATCATGACGTTATTTTTGGGGACTTATAGCTGCATCATTTA  
CCCCATATACATTTACCTTTAGTGTAAGGAACTGAGGACAGGAATTTGT  
TGATGCAGACTCTTGCTAATGAGGCTAACACTTGGAGAATTTTATCATG  
CATTCAAGAAGCTTGTTTTACATTTCTTCAATTAATACTTTAGTTGGTGGT  
TTAGCTTTAGTTGTAGGCTTATCAGATATTTGGAGATATCTTCATAAAGC  
ATGGCTTTGGTTTGAAGAGTTATTCTGAAGCTACTATTTCTGGCAATA  
ATCAAACAGCATGGCCATTTGTTTGTAGGGCTTCTTAGAATATGACG  
GTAAATCTACGTGTGGAAAAATGCTTATTTCTTCTCTCTATAAATGT  
GAATCTAGTTTGTCTTCAAATGAAATCAAGTGATTAAATGTAGTTTTC  
TAAGAAGATAAATGGAGCAAAGCACTCTGTGTTTACAGTGTGGAAATC  
ACTCATCCCTCATAAACTGTCCCACTGATCCTGACTCACATGAATGAA  
TTAAATAAAGAGTTAATAACATCAATTTACATTTTAAAGACACTTTCCC  
ATGTTTTAGACTATTGGTTGGAAAAGCTGGTAGGTGTACAATTTGTGGAG  
AGTTGGCTGTTTTTGTCTGCTGTTGTTGACGTATTTCAAAGCCATATCT  
AATTTTGTGTCAGAAATGGTCTGAATTCTACAAAATGTTGAGTTGTGTAG  
TGTGGAGAAGTACGGAGCCATTTACTGAAAGGCTGGGGGAAATGACGAG  
ACCCTGAGATAAGGCAGTAGTGGTGCGAACAGAGTGAAGGGAGGTAGTT  
GAGATATGTTGAGTAGAATCAGAATGGACATAGTGAACAACTGGATGC  
AGGTGGGGCTGAGGAAGCAAAGTTGAGGATAATTCTGAGACTTCTAGGT  
TGATCCACTGAAGTTACATTATTCAACACCACAAGGAACTAGGGGAATG  
AGAAGGCATACTGGTTTGTCTTGGAGTGGAAGGGCAGTGATGTAAGAGGA  
GTTAATGAGTTAAAGTTTGGATATGCCTGAACCTCAATTTGATATGTGCA  
CTTGATATACCTTGGGGTGACCTCCAGGCAATGGTTGAACATGTGTAT  
TTCTTAGTAAGTATAGGCATCACAGACTCACATCAGTAAGGAAGCAACA  
GCAAACCTGATTGGACGATATACCTGGAACCTCAGTACCCTATGACTGGAG  
CAAGTCTCTGTGAGTGAATGAGGATAAGAAGAATCTTGACCTTGTGGAA  
TATGTTGTTAGGAATATATGTGATGAACAACATAGGATACTTCTACAGG  
GCTCCACATGTAGTAAGGGCTTTATAAATGCTTGATAAATATTATTGTTG  
TAATTTATTTCCAAAGTAAGATGCCACTGGAGGAATCTTTGGAACCCAAA  
TTAATAACAAATAGGACTGGATGCAATGGCTCACACCTGTAATCCCAGCA  
CTTTGGAAGGCCAAGGCAGGAGGATCTCTTGAGCCCAGAAATCAAGACC  
AGCCTGGGTGACACAGGGAGACCTTGATCTATGAAGAATTAATAAAAAAT  
TAACCAGATGTGGTGGTGACGCCTATAGTCCCTGTGCTTGAGAGGCTG  
AGGTGGGAGGATTGCTTGAGCCCATGAGGTTGAGGCTGCAGTGAGCCATA  
ATTGTGCCACCACACTCCAGACTGGGTGACAGAGTGAGACCCTATCTCAA  
ATAAATAAATAAATAAATAAATAAATAAAGTACAAACCAGCAAACACTAAT  
CCTTTCTAGAGATTATTGAACTCTGGAGGGCAGATCTGAATGGAGCCAGC  
AGAGGGACCTATGGAGATCAGCCTGGCCCTGGACAGCACCAGGCAATGGG  
GTTGCTAGAGAGGTAATGGGGTTGAACAGGGTTAAGCCATGAGGTCTCA  
AGAATCCGTGAAGACTCAGACTAATTTTTTTTTTTTGCATGAGGATTAG  
GTGTTCTTAGGAATTTCAATGAGAGCAGGGTTAATGAAGGAATGCAGGGT  
AGGAGAGCTGAGGGAAGGCATCTGAGAGAGCCTGGCTTATGAATGGCTGC  
CTCAGTATGGCTCACCTGCTTTCTTGTATCTACTTAGCAGATGATCCCA  
CCCCAGGCCTCCAGGGCCAAGGTCATTTCCACATAGTCATGGGCCCTTGA

FIG. 3 (32 of 52)

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GGGCGTGGAGCAGTGTAAAGGAAGACAGAGTCTTAAGAAATTGCATTAAC.  
BTGATGGGTGCTTGGCAAGTGTGTCATCCTATGCCAAGCCTGATCTGAAG  
GGGTGCATGCTCATAGGTAGCTGCTGCCAAGATTACAGCAGCTTCTTCA  
ATCCAGATCCATGCTCTCCTATATTCAATTTTCCAGGGTTCCTGTCTT  
TCGACAGTGTAGATGCAGAAAGACTTATTGAGTTATTCTCCTGATAGT  
TGCCAACTTTTCCAAATGACAAATGGGGCATGGAGCTTGAGAGTGGAAATG  
AGGCCCTAGGGATAGCGTGCCTTAGGAAAACACTCCCAGCCTGATGTAATT  
CTGGGGGTACAATGGCATTTCATCATCAAGACTGATGTAAAGGGTGAAT  
AGCAGTGTAGTTGGGGGTGACTCGCACTGGGGCTAGGTTTCTGATTCTGCC  
TAATCCAGACAGAGCAGAAGCACTAGTGGGCTGGTAGAGGGCCTCCAGGG  
CCTCACTTAATGTCTTGGAAAAACAGCTCCAGATTGTTGGTTCACGTTCT  
GAGGACAAGCTTGGGTACTACAGGATAGAGAGAGTGGTGGGAGATGCCGT  
GGCCTGCCCTTTCGAAATGACAAATGGGGCATGGAGCTTGAGAGTGGAAATG  
GGGCATCTTGCCTTCCCTGCCAGACCTGTAGTTCAGCTGAGGGCATGTG  
GAGGCCAAATGGCTTCTTAGAGTGTACTTTCTTGAACAGCTCTGCTGG  
GAGAACTGGAGGAGCTAGCTAGTCACGGTAACTGCAGCAGTCAAAGGATC  
GTCCCGGTGGAGGTGGGGTGGAAAGGTAGAGAAAGAGAACAATATAGCGTT  
TTCTTGGAGATGTGTGGGCATGTCTAGAGGAAATACCCAATTCTGAG  
CCTTGGAGCCCTCCAGGAAACCTTGGAAATATTAGGTTAGTCATCCCAAGG  
AAGTCTAAGAAATTCTGGTCTCACCCATCTCCTTTAATTCCCACAATGATC  
CTACATGATATTAGGAACACGGGCCAGTAACCTCCAAGCAATGGATGT  
GGTGGTGAAGTTTGACCTCATGATGGAGCGGAGGTTGGTTTGAACCTAA  
CAATTTAATTTATTGTTTCAAACCTGTTCTCCACTCAGCGTTATTAAAGCA  
TACATAATTGACACATAAAAAATTGTATATGTCTACGGTGTACAATGTGAT  
GTTTGCATCTATGTATACATTGTGAAATGATTACAACAAGCTAAATAACA  
TACCCATTTCATCGTGTTCGAAAGGAATTAAGCTCAAGCACAAAAGAGAGG  
TGCTGTTGAAGAGTAGGGCTGCTCTATCTAAGTAGTATGTCTGGGGTGT  
CCTGGATCAGGCTCCTTTGTGCTAGTAATAAACAGCCCTTCTGGGGCT  
GCTCCACTTTCCCCACATTTCTTCTGGAGCCTCCCTAAGAAATTAGGACA  
TGGCCACTTTCTCTGCATAGGCTTCTTACTTCAACAAGGACAGGGCTTGT  
GCTGCCCCATGCCACTTGAGTGTCCCTACAGCACAGAGCTGAGTGACAC  
TGGCTGAGTGAGGAAATCCCCAGATTAATCTTGGTTCTAAGCATCATGG  
CTGTATTTACACGTATATGAATTAACAATTACAGCATAGTCAATAAGG  
ATTTTGTGTCTACAACTGGAATCCAGATTATGCAAAATTGGATAGTATAA  
TATTGAAATTCCTAGGACTTTTATTAGTTTTAAAAAATTATACAAGCTT  
AGAGTAAAGAAATTAACAGTGCAAAAGAAATCACTGTGAAAAGTAAATG  
CTCTGTCTCTGCTGAGAGACAGATATTGCAGCCAGATACTACTGGGGTC  
AATAGTTTTCTTTAAGCATGCCATTTTGATGGTTTATGGGACTTACAGCT  
CAAGAAGCTTGACACTAGGGTTGATCTCAGAAAATCATTGTTGCAGGTAT  
TAGATATGACCGTCTCATAAAGATACACACACAGACACAGCGATTGGAGA  
TATTCACTGGGGCTTATGGGGCTGCTTGCTCTTCTGCTCTGTGCCCTAAGT  
TGGGCTCAGAGTAGCCTGGCATCGGCTGTGGGGAGAATGCTGGCATGGGG  
TTAGCAGGAGCCCACTTAACATGTCTAAGCCACCTGGAAGAGTCTTCA  
AGGAGACCAGACTCCAGAGGCCCTAAGGAAGGAAGGACTTTTGCCCGTTT  
TTAGGTATTCTAGTCCAGAGTTTATGGGAGGAATGGTTTGGCTTTGGGTC  
GTGTGCCCCCTTACCGAGTGGGATGGGATGTGCCCATGAGCTGTTGAGCT  
GGCTCTTGGAGAAGACAGCAAAAGCGGAATAAGAGGTCAGGAAGCTGTG  
TGGTTGTAGGAAATCCAGCAGAGGGCTGGGGGTCAAAAAGTGGTCATGG  
TAGTGACGGTGGAGGCTGAGGTGGTAGAAAATCAGAGGACAAACCCCATG  
GGCTGCTGGTGATCTGACCGAGCTCCTATGCTCTCCTGGTTCAATTTAGG  
CTCTGTAGCAGCAGATGATTGGCTGGTGTGAGAGCAGTGACCTGCCATA  
TCAGGCAATCCAAGACAAGTCCAAGCTACGCTGGGAGGAAACCTGAAGGC  
AGCAGCAGGTAGACTGGCTGAAGACAGACAGGCAGGCAACTTGTCAATCA  
GATTTGTGTTTTAAGGACTTTTAACTGGGGAGCCCTCCGGGACAGATCA  
GATGAGAGTGAATGTGCTCCGCTTAGCC

>Cont:ig37

GGCGCTTCGCAATCTGTAAAAGGGAGAGTGGTTTTATTTATTTTAAAC  
ATAGTCAAGCTGCTAAAGTATATGATATGTATAGATAGAGTATAATTAA  
TACTTTCAACTACAGACAAAATCAGGAGAATGGAATTAACAAATTTA  
CAATGGGTAAATGGCAGCATTGGGTTGCGCCCAACCCACGAGAAGGCAGAC

ACCAAGATTCTAAGATC...ACGTGGCCAGCACTTCAGACTTCAAATAGA...  
TTCGTGATTATGCATTATTTTTCTCGGAAAGTTTTCACTTCACTATATGC  
TACTTGACACTTGTCTTCTCCTAAGACATCCCTCTATTTTTGAGATGACTAA  
CTCAGCAATTCAATTTCTCTCACGCATAAGCTGTCACTCAACCCAAACCCA  
CCAAGCCTGCATTCTACCCTCAATAAGGTCTTGGTGTGTAAACTGACCCA  
CTTCACCTAGTTCTTAGCCCTCTCTTGACCAGACATGACTCTTTCATAA  
GCTAGACCTATAAAGTCAGGGCTCTTAAGTAGCTGATCTCTGATAGTGCC  
AAGTGTCCSSCACTGTTTCAATTTTCCACTCCAGCTTCTAACAGGTGATA  
GACTGCTTTTTGGGGGTAGGGGCACCAAAACATATAGACCTCATGTTTG  
ATGTAGACACTCCAGTTTCTTTAAATTACAACCTACATATTAATAATGACT  
TCCAAGTGTACATTTTCACTCCAGATCTCTCCCTGGATCCCCAACTTTGT  
AAAACCCACCGCTTATTTGATATCTTTTGATGTCTGACAGGCATTTCAA  
TTTAATACTGTCAAAACAAAGTTATTGATTTTCATCTCTGCATCTGTTA  
CAAATTTTTCTTACTTTGGTAAATAGCACCCAGGCTGTGTCACTGCCAA  
GAATTTTCCACAGCTCTTGAATAAAATTCAAATATTTTCCAAGGCAGA  
AAGGCACAGTGTAAATCTGGCTCCTGCCTACCTCTCCAACCTCGTATCACA  
CTAGTCTCCCTGTCACTCACCCCTCCAGGAGCTCAGGTATCCTTAAAGT  
TTCTTTTCTTTTTTTTTTTTTTTTTTTTTTTTTTGAACAGTTTTGCTCTGTT  
GCCCAGGCTGGAGTGAAGTGGCATGATCTCAGGTCACTGCAACCTCCGCC  
TCCCTGGGTCAAGTGATTCTTGTGCCTCAGCCTCCCAAGTAGCTGCAATT  
ACAGGCGCGTGCCACACACCCGGCTAATTTTTGTATTTTTAGTAGAGAT  
GGGGTTTTCAATGTGGCTAAACCGGTCTCAAACCTCTGACCTCAAGTG  
ATCTGACCACTTCAGCCTCCCAAGGTGCTGGGATTACAGGCGTGAACCAT  
TGTACCCCTGCTCCTTGAAGTTTCTTGATCCAGACTCATTCTGCCTTAA  
GGTCTTGCATCTTCAGTCTCCTCCCTCAAATGACACCTCCATGAAGACGCA  
ATTACCTGTAATTACCGTGTCTTATTTAGTCAATGTGTTGGTTTTCTGTC  
TCCCTCACTACAGTGTAAAGCTCTATGAAGGCAGAAACCTTGGCAGTCCAG  
TTCCAGCACAGTGCCTAGCACACATAGGTATTTAATAACACACAGTAAA  
ATTACCTTTTAGTGTGCAATTCTGAGTTTTGACAAATGCATCAAGTCAT  
TTAAGTCTGACTATTATCAAGCTATAAGATGGTTGCAACACTATCACTAA  
TTCCCTCATGCTCCTTGGTAGTCAGTCTCACCCCTAACGCCCCCTCCTG  
GCAATCACTGATCCGTTTTTTGTCTTTATAGTTTTGGTTTTTCCAGAAATG  
CCAATAACTAAGTTTTGAATGAATGAATGCTATTAACTCTCATTCTGAC  
TCCAGAGCAACATCCATGCAATATTTATTATTTCAAGCCCCAAATACTGCC  
CCCTCACCTTCAGTCCCAACCACTACTTGATGATACAAGGTGAGACATT  
GGCATGTGCTTCTCCATGTTTCTTAGCATTTTCCCTATCTCCTTAGCCTT  
CCTTCTAATCATAAACGAAGAGTGAACCTTCCCTTCTAAAGGCAACTTA  
CTCCTAGGACCTCGATGCCATAATTTGTTTCTCTAGTACTTTCTATATA  
TACACCAACAATTAGCTCCAGAAAGGTAAAGACTCACTGTGTGCTCATC  
ACTGTGTCTCCTAGCGCTGGCACACTGCAGGTGCTGAAGAAACACCTAC  
AGAATGAGTGAATGAATCTCTCCCTCTCTAGACTCCTTCTCTTTGTAAAT  
CAAACATGTTCAACTGCAACACAGTCTTATGACCAATCCTCTGTTGTCT  
GACCTAGGCTGAGCTCCAGGGCTGGGACCTGACTTCTTATTACCACC  
TCAAGGTCTCTGCACTCACTTCTCTTCTGCTCAGGATTGTTTTCTTCT  
TGTCAACAGTCTTTTCTCAGACTTAGGTCTCAGCTCAGACATTGCTGTTG  
AAAGTACTTCTACTGATCCTTTTATCTAAAGCAGCCATTCCAGCCCTACT  
CTCTTGATCATAGCACCCCTGAATTAAGTTGTTTACTTACTGTCTCTTCAG  
GAGGGCAAGGAGCTTGGTGGTGGTGTTCAGGGCTGTACCAAGCTGTACCT  
TGCTTACCCTGCTACACTTTTTAGCAACCATCTAATTTTACATGCTCCC  
TTCAGTCTGTCAGAAATTTCTTATTTTCTACTTCAAGCAGGTATACATAT  
GTGCTTCTCTGGGAGGCTCACCCACTTCATGAGACTACATTTGGTCTG  
GGTAGAAAGGTACAAAATCCACTGGCTCAGTTTTAATCAATGTATGTTA  
ATATTAACCAACCTGAGATCTTGATTTCCACGCCTGGCTAATTTGTATT  
TTTAGTAAAAACAGGGTTTTCTCCATGTTGGTCAGGCTGGTCTCGAACTCC  
CGACCTCAGGTGATCCGCTCACCTCGGCCTCCCAAAGTGCTGGGACTACA  
GGCATGAGCCAGCGTGCCCGGCCTAAGATCTTGATTTCTACCATCTGAAC  
TCTGTATTTGAAGTACTGCTCCTGCTTGAGCTTACTGGCCAAAACCTTG  
CCCACTCAGACTCACGGAAGTTTCTGGTCTTCCCTGGTAACTTTCTGA  
ACTTAACCACTGGTTTGCTTGACAAGAGATTACCATCTTCTCACTTCCTA  
GCTATGTGAACCTACTTATCTGCTCTATTGCTGTTCAGTCTAGCACGGCA

FIG. 3 (34 of 52)

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CTTATTGAACGAGTGTCTACATCTGCACCCCTACTTCTTACTCATCCAT  
TCTGTTTCAATTTCTTAAAAAGAAAAAAGCTATTGTAAACATACG  
ATTACAGAAAATGATTTATAACATGTGTATGTACCACCTAGCCCTGTCAA  
STCTTAATATTTGTTATATTTGCTTCAAATCTTTTTCAGACTGTAGTTA  
AAAATTACTTAGGAGCCATTATTTATGGCCTATTTCTGACCTAGTCTTC  
TTGATGGTCAATTTGCCTAATCATCTTAAGTTGCAAAAGCTTAGAATTAA  
AGCAAAGTACCTTCGATCCTCTGCTGTTCCTTCTTTTAAATATTTGGGT  
TTGTTTGGGTCCCATTTACGGTTGTGACATCAGCTTGAGTTTGGGAGCT  
GTCTTGTTCAGAAAATGGTTCTGGGGAACAGCCTTTTCAACTTGGAGTC  
CAAAGTCTGTGCTTTTGTCTGAAAGCCATTATTGTTATGTTTATTACCAC  
TGGTTCCATTTGGTCTTATGCTAGGGGTGCTTGGAAATGGCTGAATTAAT  
CTGCCAAGTCTCAAATTAGGCCTCTGGCTTACGGCTTTTGACTTTTGCGAG  
TACACATGATGTCTGAGGTATACAACTTGGCTGGACTTCTGATCTTGCT  
TGATGTTTGGATGTCTGTTGTTATATTCACCTGAAGCAAAGTGGGTAT  
GTTCTGGGTTTGGTGTGCTTCACTCTCTGTTTCAAGTAACAGGGTATGACC  
TATCTTAGTTTCATTTGGTCTTTCATATTGACTCCTATTAACCTTTATAT  
CTTTGATGTTCTTGACTACTGGTTTCTTTGATGACTGAACTTTACTAAGG  
GTCCGAATAAAGTGAGAGGGAACCGTCTTTGAGGGTTTTACTCCTGGTCT  
TGCAAGATCTGCTCCTCTAGAGAGTTGCTGTGATTTTACTGGGAAAGTCC  
TGCTTTGTGTTTCTTCCAACAAATTTGTTTATTAACCTATCTTTCAGAACA  
GCCTATTAAGTGAAGCTTTTGGCCAAGGCTTGGTTAGGAACTAAAGTGT  
CTTGGTTTGAATTATAAGAGTCAGTCTTTGGCTTACTTCTGGTATATAAT  
TAGGATCTGGCTTCTCTCAGGTTCTGTTAAGATATCTAGCAAGTTCTCT  
TTGTTTGTGTTTCTTTAGAAAGTTATCCAAGATTCTGTTTTCAACATGGAT  
ATTATTCTAAAGTCTATACATTTACCATTTCTTGATCTGTTAACTGCT  
GCTTTGTAGTTTTCAATTGCTCTATATTAAGTGACCCACAGGTTTTCTT  
GACAGTCTCTGTGGTGGACTATCTAGCTTCACTGTTGAAAAGTCTT  
GCTGAAAAGCTTAGACTATGGGTTAGAAGAAACACATTTTGAAGTCCGCC  
TTTTGCCCAGAAGTTTTGGTGGCTCTAAGTTGAGTCTGGGACCCTGCA  
GTATTAGGTGGTCTGGGCTGGAGTTTAAATGCTGATGGACCTTTTAGGTTT  
GACAGGCAAAACAACATGGTTGGTAACATCATTTTGGGTCTAATAGTCT  
GAAAAACAAGAAATACATATTAATAAATCTTAAACATATCTTATTGT  
TTTTAAATAAATACTGTGTTTAAACATGCTAAAAAATAATCATTTTT  
AGAATTTCTCTAAGAAAGTTGAATCCTCAGAAAGTAAAGAAAGACTCAC  
TAATAGGTAGTTTTTGTGTTTTTTTTTTTTTTTTTTTTTGGAGACAGGATC  
TTGCTCTGTACCCAGTCTGGTGTGAGTGAATCTTGGCTCATTCG  
AACCTCTGCTCTGGGTTGAAGCAATCTCCACCCCAACCTCGCAAGT  
GGCTGGACTACAGGCGCATGTCACTACACCTGGCTACTTTTTGTATTTT  
TAGTAAAGTTGGGTTTTACCATATTGGCCAGGTTGGTCTTGAAATCCTG  
ACCTCCAGTGATCCACGCACCTTGGCCTCCCAAGTGCTGGGATAACAGG  
TATGAGCCACCACACCTGTCTTAACAGGTAGTTTTTACAACCTGAGTTCC  
TATCAGAAGTATATTAGAATCTTTAGCTTGACAGAATTAAGCAGAGATG  
CAGTGAATATACAAAACCTTGCTCTTTCAAAAATGAATTTGCCTCAAACAG  
TAGTTGTTGAATGCCTATTATATCCTAAGTGCCCTCCAAAGAACCCTGAA  
AAAATACATACATAATGAACCTTATGTTAGGGTACCTCCCAACAAATCTCT  
CCTAGTACTTTGTATAGCCACACTATATGTTTTTAAACCACTGCCTTTG  
TAAACATCACAGTATCACTCAAGAACCTCTGTCTCATCCCTGGAGATCAG  
TGACAAGGAGATAGGTGGCAGATGATGTGAGGCCTGAGATATGCTGCCAC  
AGCTCTCAATAAACATGTAACATCTTAATAGTCATATTTGTAAATCAGC  
CAGGACAGGTTTTTAAGGTTAGAGTCTATGTTAATAATAAACAAATGTTT  
AGTCATGTGATTTAAGTTTGGATAAGAAAGGTAGGACTCGATTACAGAGA  
ATTTTGAAGTACTAGGGAAGGGAGTTTAGAATTCATATGGTAAGTAATTGG  
GCAAGCCACTATGAATTCCTGAGCATCTCTCATGAAAGCAATTACTCAGA  
AAGGAGAATTTACAGAGATTTATGGAATATGTTTCCAGGGTAAGATATG  
GGAATGCTAGAGTTACCACTCTATTTTTGATTTGACAAATATTGTGAAGA  
ATCACTACATAAACTTGGCGAGTATGTAAAGGATTTCTAACCAGAACCAT  
TTGGCATTGAGGGCAAAGAAATGTCTACTCTGGATGATAGCGGTGTGTGT  
GGTGTACTAGGAGTGAACAGCGGAGTTGGAGTGGGAGGCAGAGAGAT  
GGATGGTATACCCACAATGGCTATATCTGGATTAATCTTTGAGCACCAAC  
ATTTATATACACCTCGGATCTCTCCATCATTTGCTTACTGAAGAGGTGGAG

FIG. 3 (35 of 52)

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GGACGTTGGCATGAAAGCTCCAAATGTGTTTTTTAGTTGCTTTCTTA  
ATATTA AAAACGAATTGATATAATCCACAAACCATAAAATTCACCATTTT  
AGTAAGTGCACACTTCTGTGGATTTTAGTATAGCCACACTATTATACAGC  
AATCACCACCTGTCTAATCCAGAACATATTCATCACCCTAGAAAGAGAC  
TTGGGTTTACTTGTGGCAGTCCCTCCCA  
>Contig38  
GGTCTACATGTGCTCGCAAGATTGGATATTGAAATATCAGCAAGAAATTA  
AATGACATAGTAGTCATTATGCCTAAATTATTGTTATTTTTTGATTGAAA  
AAAGTTGAATATTTCAAATATCAAGGTAGTAGTGAGATATAATAAGAGA  
GAGTCAGTTCTAAGTATAGAATTGCTGATTCAAGCTCTGTTCTCCA  
ACATTTGGGCCACATTGAAGAGACCATGTAGCTGCTTTCAGCCTCGGTTT  
CCTCCTTTGCAAAATGGGGATTACACTACCTGCCTCACAGAGATGTAAAC  
TTATGACATGTTATCATGATTGCCAGGGCCACCTGTTTTCTTTTAAACA  
TTGAAATCACTGTGCCTGAAACAGGGATTTCCCTGCCCTTTGTGCAAGCT  
CCAGAAACAGGAGTCAGCCTGAGTCCCGCAGCTAAGAACGTGGATTCTGG  
TCATTTTCTCATAGCGAACACACTTTCAGAGTCTTCAAGGGAGTACATT  
TTCCTATAACTCACCTTAATCTCAGTTGAAGCCTCGTTTTCTTATTTGCA  
CTGTGGCCAAAACTAAATCTCATTCTTTTACGTAAACTTCAGCAATTC  
AATAATAGTACAGTCATTTTATGTTTCAACTGAACCAAGTCAGGGTTCCA  
CTCCTGCCTCCCTTTCTGCTCTGAGGACATCCATGAAGTGGAGGGGTC  
TATGTAGCCTGGAGCTATTGGTGAGGGCGATGGGTCCGTGGTGGTCTTG  
GGAACTCGCGGGCTGTGCTGTGGCTGGTCTGGTCTGGTCTGGTCTGGTCT  
GTTCCACGCGGGTTCAGCTGCAGGACAGTTCGTGCTCTTCTTGTCTTAAT  
GATCAGCTTTTAGGCTCACGGCCTGTCTCTGCTGAGATATGGAATAGGA  
CAGCCTCTGGATCTTCTTAACTCTCCTGGGGCCACAGGGGACTCTGTT  
TGTGCTGTGCCCCACATAGGATGATTCTGCCAGACCTTTGCTGCCATTT  
CTTGCTGTGCTGTGTTTTAGTCTCTGGAGGGCTTGCAAGTTTCTTGGG  
GTCCCTGTGGAAGCAAAGCAAAGTCTCTCCAGCTCAGATGTCTAAACG  
TATCTGGGTTTTATCGTCCACCCATCCAGAGCTCAGTCTAGAGGAGGGG  
GCAGCCTTCGGGTTCTCTCTCTCTCCAGAGCCTCTCTCTTGCACCAG  
GGCAGCCTCTCTCTATCTGTTGGAAGGGCTGTCTGGTTCTTGAATATAG  
AGTTGCAGGTTTGAGGGGTGTAGGCTGAGGTAAGGCAAATATCACATGG  
AATAAAATTACCCTGTGTCAAGGAACAACAGAGCTGGACAGTTTTTAA  
ATGTGAAAACCAATTTTATTAGGACTATGGCGAGAGGTGAAGTAAGACC  
TCAGTATAGAATGGGCTCAATTCGAATGCAGCATGGGCAAATGGGAAT  
GTATAGCCTAGGAGCAGGGTGGGAACCTGTGGATGAAGAATTACTAAAAG  
GGCATATCAGGGGTGAGGGGCGTCTGGCTACACCCACTAACTACTGTT  
GCTGAAGAAAGGCTGGTGACATCACTGGGAATGGTGGGGATGAAGAA  
TCCAATCAGATGGATATTGAGGATAAGGGGATCTTGATAAACTGGCTTAG  
CAGGGTTTTTGTCTAAACTGGTTTTTCATAGGTAAGTCCACAGACAGGTCT  
TGGAGAAAGTTTCAAGGACCTACGGTTTTGTTCCGGGCAGATGCTTTGTCTC  
TGTCACTGGCACTGTCACTGGCTTTCTTTAGTCCCTCCCCCTTT  
TTTTTTCTGGAGTAGTTTTGGGAGACCAGAGGAGCAGGGAGTTAGGGAG  
AGTAGTCAGAAAAGGCCAGAGAAAATAAGGAGGTGTCTGTAGGGAAAATC  
CTTAAATCCTCTAATTAAATTAATTTAATTTATTTATCTGGGACAAGGTC  
TCACTCTGTTGCCAGGCTGAAGTGCAGTGGTGTGATCTCGGCTCACTGC  
AGCCTCGACCTCAGGGCTCAAGCAGTTTTGCCACCTCAGCCTCCTGAGTA  
GCTGGGGCTCACAGGTGTGCACTACCATGCCCGGTAATTTTTGGGTTTT  
TTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTGTAGAGATGAGGTTTCGCCATG  
TTGCCAGGCTTGGTCTCGAACTCCTAAGTGTATCCATCCACGTCCGACCTC  
CCAAAGTGCTGAGATTACAGGCATGAGCCACTGTGCCCGGCTAAATTCT  
CCAATTTTAAATGCTTCCCTGTTCCCTGTTCCAGATTTGGGATATTGAC  
TGCTGTTAAATCAGCGATTTCTCCCTGTGGAGAGGTAGCCAATAGGAAGC  
AACAAGAGTGAGGAGTCTTATATCGAAATAGAGGGTAAGAGAAGAGACA  
GATGTTATCTTGGCAGTGATTTAAGAACAGCGAGTCTGTAAGCAAAGCAA  
AGCAAGGCTCCAGGTGCTGAGAAACAATGGCTTTCTGGGGAAGCGTCTG  
TGTTCAAGACCTTAAGTTGGAACATCTCTGAAGATGTTGCCATGAAGG  
TTTTCTTCTGAAGTTGAGTCTTTCATCACTAGGTAGGCGTGTGTTGGAGT  
CTCTATCAAACAGATCCTGTGTTTATTAGGAAGCTGTGGTTCATAAAGCC  
CCATGCTAATTTTGCAGGTAGCAGGGTGGCCCTGGCCTGACCCGGGAGCA

FIG. 3 (36 of 52)

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SAGTGGCTGTCTCCCTCCCTCAGGCAGGAACTCTCTCTCTGCCACCTAGTCTCTG  
CTGCATACCCACATTTCAAGGGGAGCTTCTGGGTGGTGAGTTTACCAGACT  
ATGGTCTGAGGTAGAGTTAAGCAAAACAAACTAAACTGCATAAAGAAAC  
AGAAAGAAAATCAGGTGTTTATAAAAAACAATTTGGCATTGTGTGTGTTC  
AGCTCCGTGTCTGATTTTATTGCTTCCACAAATAGTGCCGATATGCACCAGG  
CACTGTTGTAAACTGAAAATATGTTTTTGGATGTGCCAGTCTGTGAGT  
ATTAAACGATGGTTGATTTGAAATTTGCTATGATTCAATTTCTGGGGGT  
AAGATGCAGGATTTCTTTGGGGGGCCTACGATGTGGCATTCTAGAATTCT  
CAAAGAATCAACCCTGGTGGGACCAGGAAGAGCTGAGCTGAGGCCTCTCT  
GCTCATGTGTACTTACTGGAGATCATGGAGACAGGTGAGCCTGAGTGCAC  
GTCTCACCAGGACAGCAGAGGGGGAGGAGGCGGAAAGAGAGCTCTCT  
CCATTTCTGAGAAGTTAATGGTAACAATGGCATAACATACTACTTTACAG  
TTGAAATTGAAACCAAGCATTAAAGTGTTCCTAATGAAATTTGGCAATT  
TGGGAGTTTTCTGAGCTGCATTGGATGTGGTTTTGTCATGCTGTTAGGATG  
AGCAAGAGATGATGGAGAACATCTTCTTTTGGAGCTTCTCTTGGACGTG  
GGTCACTCCCACTCATGGAATTAGAAAGCTTAGACCTAGACTTGAATCTC  
ACCTTCTCAAGGTGCTCCCGGGCAAATCACTTAAGATCCATCTTCTCTC  
CTCCTGCTCCTTCTCCTCCTTCTGAGTTTTTTTTTTCTTTCCAAAATTC  
AAATGACACGGTACTGGTAGAAGAAAAGGTCCAAGTCTGCTTTTACAGCT  
CCCCCTCATCCCCAAATGTACTCCGACCCCAAGATGACCATGTTATCATTT  
GATTGACATCCTTCTAGTTTCAACTCATTTCTTTGCATGTATATGCACGT  
ACATATACACTATTTTATTTTGGCAGGGGTACCGTTTAGCTGCATTAAT  
TTCTTATAAAATAATCTATATTTACTTATGGTTTACGTAAAAACAACATAC  
ACATGTAAGTGTATAGCTTGATAAGTCTTCACTGTAAACCAAAAAATAAA  
TTGGAAGCCCCCAACCGTCTGAATGGACCCCTCTTCTTGGCCAAGAGC  
ATTCCAAAGTTAACCTGAAAAAAGTAGTTCAGGTGATGGAAGGGAAG  
GTTGGACATGCCCCAGTATACCTTCTCCCTTTTGGAAATTCAGGAAAAGC  
TGACCAGCATTAAACATCAACACAGACCTTATGTCTGATAGGAACTTTGA  
CAATCTATTCCCTCTGAAGCTTGCTACCCGGAGGCTTCATCTACAAGATA  
AAACCTTGGTCTCCACAACCGCTTATCATAACCCAGACATTCTTTCTGT  
TGAGAATAATTTACCTTGTAACTGGAAGCTCCCTGCTTCAAGTTCCTC  
ACCTTTCCAGATTGAACCAATGTAAACCTTACATGCATTGATTGATGTAT  
TATGTCTCCCTAAGATGAATAAAAGCAAGCTGTATGTTGACTGCCTTCAG  
CACAGGTTGTGAGGACCTCCTGAGGCTGGGTACGGATGCATCCTTAACC  
TTGGCAAAATAAACTGTCTAGATTGACTGAGACCTATCTCAGATACTGTT  
GGGTTCAAATATATACTTATGAACTAATAACAAAAATCAAGTCATAGAA  
TATTTCCATCACTCCTCATCTACCCCAAAATTTCTTATGCGTCTTTGCA  
STCAACCTCCCACCCCATCCCCAGGCAACTGCAGATCTACTTTTGTCTC  
TGCACCTTCAACTGACCTTTCTGTGATTTTATATGAATGGAATCATGCG  
CTGAGCAGTCTTTTGTGTCTGGCTTCTTTTGTCTCAGCATAATGTTTTGA  
GGTTTGTCCATGTTTTTGTGTTTGTCAATGGTTAATTTCTCTCCATTGCA  
GAGTAGTTTTCTATTGTACATGTGTACCACAATTTGTATATCCATTCCAT  
TGCTGATGGACATTTGATTTGTTTCCAGATTTTGGCAATTATGAATAGAG  
CTACCATGAACACCCAGGTACAAGTCTTTGTGTGGACTTATGTTTTTCAAT  
TCTCTTGAATGGAAGTGTCTATCAATAAGTATATGTTTAACTTTGTAA  
GAACTGACAACAAATATCTGCGATGGTTATGCCATTTGTTTTTCTAC  
CAGCAATACACGAGCATTTTCACTTGTCTCCACAACCTTTGCCAAAACCTGTT  
TTCTTTAATTTGGACATTTAAGTGGTGTACAGAGGCATCTCATTGTGGTT  
CTAGTTTTCTTTGCCCTGATGACCAATGGTGTGAACATCTTTTATGTG  
CTTTTTGACCATTTACATATCCTCTTTTGTGAAGTGTCTGTTCAAATATT  
TTTGCCCATTTAAACATTTGGGGGTTTTGTCTTATTATTGTGTTGGGAGA  
GTTCCATATTTATTTATTTATTTAGATGGAGTCTCACTCTGTTGCCAGG  
CTAGAGTGCAGTGGCGTGATCTTGGCTCACTGCAACCTCCACTTCTGGG  
TTCAAGCAATTTCTCTGCCTTAGCCTCCTGAGTAGCTGGGATTACAGGCA  
TGTGCCACCACACTGGCTAAGTTTTTGTATTTTATGATAGATGGGGTTT  
CATCATGTTGGCCAGACTGGTGCCAAATTCCTGACCTCAAGCAATCCACC  
TGCCCTGGCCCTTACAAGTGCCTGGGATTACAAGCATGAGCCACTGTGCCT  
GGCCCATATTTATTTTATTCTTTATTTTGTATACAAGTTCTTGGTCAG  
ATACAATAATACCTGGTCAGATGAGATAATGAGTTGGAAAATGCTTTGCA  
AATGGGGGAGAATAATTTAAATGTTATTTATTTATTAAGAGCAGAGGCCC

FIG. 3 (37 of 52)

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TTCTCTTGGCGGTAC...AAGCCGTTTGCTTCTTCTGCCTTTTATAAA...  
AGCAGAGTCGAGCTACACAGGCTGTCTGTGTTGGCTGCTATTAGTTAATC  
AGAGAGTCTTTTCTTTCCTTGCCTTGTCAATTCTAATTTGTGACACATAATT  
AGCCACAATATGTGTTTTAGTTGTGACACTGGCCTGGGAAACCAAGGGA  
TGTTTAGAGTGGATTTCCTTGATTGTTGCAATAATTGTGTGTTTTCTGCA  
TCTTCTGTAAACACAAATTCATGGAAGCAAAACATGGAAGCAAAGTACC  
CTGGACATCCCCCTTCTTTATGAAATTGATTTCTCTTAAATGTAATGTT  
TGCTTGTTCCTTACTTTAAAGCAATTTAAGAGTTTATTGAGAAAGTGA  
GCCCTGGAAACATAGATGCATAGAGAGAAAATTCTACCACCCTCAGGTCC  
CTATTGTCTTCTCTCATAAAGTGTAGTTTCAGGGCCTTTTAGAAGTTTCT  
TTTCTGCTCTGATTTGCATGTTTGTGAGTGTGCTATTTTAAGTATTTGG  
ATTTGGTCTGCAATCCTATGAGAGATGGCAACAGAGTAGGGATCTCAA  
GCCTGCAAGTTGTATTAAAGTCCAGCAGGGCCTTGTATTTACAACAGAGGG  
TCCCTGAAGACATTCCATATATTATGCTAGGGGAGTGGCCAAGCAAATTT  
TAATGTGTCCCTATGGTGGGATATTTGGGGTTAATACCTGCCCTTCTCTT  
AATTTCTTTTCTTTTCTTTTCTTTTCTTTTCTTTTCTTTTCTTTTCTTT  
TGAGTCTTGCTTTGTCAACCANGCTGGATTGGAGTGCAGTGGTATGATC  
TCAGCTCACTGCAACCTCCACCTCCTGGGTTCAAGCAATTCTCCTGCCTC  
AGCCTCCCAAGTAGCTGGGACTATAGGCACACACCACCATGCCTGGCTAG  
TTTTTTTTTTTTTTTTGAAACNGAATCTCGCTCTGTGCGCCAGGCGGGA  
CTGCGGACTGCAGTGGCGCAATCTCGG

>Cont: 39

CGCTCGCATCCCTCATATCCATGAGTGTCTCTGTGGGCCCTGCCTCTGAAA  
TAAATCCTGCCTTTGTCTCCAGTTCACCTCCAGCCACCCATCCTGGGGCT  
GCACCTCTCTCTTCCAAGCCCTCTCCCTTCTCTTCTCTGGTGTGCTGT  
CATGTCAAGCATATGCATCAGTGGCAGCAGGACATTTGAAATGCAACCAG  
TACAATTGGGCGCGGTTATGCCTACCAGTTTTCTTCTTAAACATTTTA  
TATTATGTTTGAAGCATGCCACCTTTCTTCACTTGCCAACCTTGACAGA  
TTTATTAGTTTGACAACATCCGCTGATAGCATCAGTAATAAGTTAATTGTT  
TTTGCAATGTAGCTTTAATTATTCTCATTATCATTTATAGGAGTTATTC  
TTTGTAAGGGTAACTGAGTTTTCAAAAACAAACAGAAATTTGGGGTGGG  
CCCATGGAGCGTGACTCATGAAATCAGATTCTTAGAAGGACCTCGGCAAG  
TCTCTGGGTTGCTGTTAATGAGCCTGGCTGGCTGCCAGGGGTGTGTCTGC  
CCTTTATGAGGCCACCACTGTTCAAATGCTTGCTGCAGCATTACTTGCC  
TAGGTAGTGTCTGTTTCTACTGAACTGTGAGGATCCAATCTTTGTGGT  
CTAAGTAAACAATACTCAGATTCACAAGGAATTGATTAATAAGCCAGAATG  
CCAAATGTATTACATTTTGTGAAGACCATATTTACAGTGATTGTATCTG  
CTCAAGCTCAAATTAGGATTAGAGTTCTGACAAATACATATGTGAGAAGT  
ATGAGGTTAAATACTTGAAATTTGGACTTTTCTAGAAAATCTGAATGTGA  
TTGCCATTACATACCTTTCTGGGGATGATGATTCTTGACTTTTATTTT  
AAAAGACATAGAAAATACTTAAGAATCAGATTGCTTGGCTGGGCACAG  
TGGCTCATGCCTGTAATGCCAGCACTTTGGGAGGCCAAGGTGAGTGGATT  
GCTTGAGCTCAGGAGTTTGAGATCAGCCTGGGCAACATGGTGAAATCCCA  
TCTCTACCAAAAATACAAAAAACAACCAAAAAGAATAAA  
TTAGCTAGGTGTGATGGTGCCTGCTTGTAGTTCCAGCTACTTGGGAGGAT  
GAGGTGGAAGAATTGCTTGAGCCCAGGAGGTGGAGGTTTCAGTGAGCTGG  
GGTTGCAACAGTGTACTCCAGCCTGGGCGATAGAGTGAGACTCCGTCTCA  
AAAAAATAAATCAGATTGCTTTATTGCTGGTTTTCTTTCTAAACTGA  
GATTGGGTCCCATCATCCCTGGCCCCCATTGGTTAATGGTTCTCTCTTT  
GTCTATTGAATAAAATACAGATGTCTGCTTTTGGCAACATGGTTGAATGT  
AGACACTGCAGGGTCTTCTGACTCAAAATGAGTAAGGCTTAGATAAAAC  
ACATTTTGAAATGCATTTCTGGATGAACAGCAAGGAAAGGAGATCTCTTA  
AAATCCTCTTTCTGTTCCCTCTCCCTACCCCTCCAAGTGGCTTAAGT  
AGGAAGGGTGGTGAGCGGCAGGTAAACACACGTCAAAGGCAGTCTTCCTC  
TCTGAGGGAAAACACTTGTATAAGCATTGCAATCAATGGGCTCTTTAAT  
TATGTGCCAGTGGCAAGAGCGGGTGTGAACCCAGGGGCTGCCTCAATC  
CGGGGCTTTGAGGCAGAAATAAGTGGTCTCAGGTGTGTGGCATTCTCTT  
GCCCTTCCACCCGAAGCAGACACAAATCCTCTCTGGAGGCAAGTCTCCCA  
ATTGAGCCAGTACAACCTCCACAGACTAAGATCAATCATGTACAAGCTCA  
CAGACAAAGGTCAACCAACACACAGAGCAATAAACAAATTCATGAGTGAC

FIG. 3 (38 of 52)



GTGAATGAGAATAAACA...AACAATAACCACCAGCTGGGATGCTCTAAG.  
CTTCAGCTGTTAGAATTCCCTGAATATAGAATAAACTGCCACAATGGCAA  
ACATGCATCTAGTACTTACTGTGTGCTGGGTTCTAAGAATTTTGCACATT  
GTGCCAGATACCGACTCAGCTTCACACTCACCTCCTACTGTGCCCTCTT  
AATTTGCACTAGATTAAAAGGTAGAAAGGAAGAGGCAGCTATTCTGTTCT  
TGGCTGTGCCCTCTGGCAGCACATGCAAAATGGGCAGTAACAGTGGCAGTC  
ACAGGTAAGTAGCCTTCTCACAGTGTGGAGTTAAAGGCATGGGACTGAGA  
CGAGCAAGGTTCTTAAAGGGACAGTGGCCAGTAGATGACCAGGGGCTACT  
GGAGTGGCTGCATGGCTCTGTGGAAGCTCAGAGGAGCCTTGGGTCTTGCA  
GGTGCAGTAGCAGCTTCTGTAGTTCCTGATCTCTGGGTCCCACAATCTT  
CCCCGTTTTTGTCTCCTCCACTTCTAATTTTGTAACTGACTTCCCTGTGTG  
TACTTCTCTCTGTGATTGAAATAGCCAGACTGGTTTCTGTTTCTTGATAA  
GACATTGTCTGGTACGAACACAGTAACCTATTTAATCCGATATCTCTATG  
AAGGAGGTACAATAATTATTCCTATTTTACAGATGAGGAAACACAGCAGA  
GAAATAAAGTCAATTGTCTAAGGTTGCACATTTAGTCAAGGGAAGGGTTG  
ATATAACATATAATTATTTAGAAAACATCTAAGGAAATAAAAGGCATAAT  
TAAAAATAAACTAGGCAGGTTTTAAAAAATGAAGTAATCTATAAGTAA  
AAAAGTATAATTGTTGAAATACATATCTTAGTGGATGGGTTAAATAGCTG  
AAGAAATGATTAATGAACCTGGAAGGTAGTTCCTGAGGAAATCAGAATTCAG  
CATAGATAGAAAAAATGGGAATTTACAAAAGTACACAGGAATTATAAAG  
AGGTTAAATTATAGGGAGGGTAGAATGAGAATTAACATTGGTCTAACTGG  
AATTTTGAAGAAGAGAATAGAGAGAATGAACAAGGCAATATTTAAAGAG  
GTGGCTGAGAAATTTTTCAGAACCAACACAACTATGACTTTACCAGTAGA  
GAAAACAATGTACACTGAGGAGGATAAATAAATATACTATGAACAAATTG  
TAATAATAACTCAACAAAGACAAAGAGAAGATGTTAAATCAGCAAAA  
AAAGAAAGTCAGACTTAGAAAAGAAATGCAATGGCAGACTACTCAACAAC  
AACAAATGGAAATCCAAATTCGGTCAAACAGTATTTCTTCATGCTAGCATA  
TAGC

>Contig40

GGGAGTCCGCTATGCTCCTAAAGATTTGCACCTCTGATCTGGTTTGTAGT  
TAGTCTCTTTTATGCTTTATCCTACTCAACTAATTTTTTTAGTGCCTGT  
TTTTTTTTTTTTAATGTGTGTTGATGACTACAATCTAAACTCATTCTA  
CTGATTATGGGTGCTTTAAATCTGAGCAGTCTTTCGCATTTACTGCCT  
GTGATGGCCCATCCCACAGCTAAAGTGTGTGGCCACTGCTTACAGCACC  
ATGTGATAACGAGTAAGGGAGAGATGCCGCCAGACTCTTCTAGGAGCAG  
CCAGTAGGACCTTCCAGGGGTTGCAAGCAAACACAGCAATATGTGGAGT  
GTGGCAGAGSATGGCCCAAGAGGATGTGGCAGCGGCTAGTGCAGCTCAG  
CTTAGTCTGAGAGGAAATGCTGGAGAGGAGAGCCAGTCTGTACAGGCAT  
GACAGCCCAAGGACTTCAACAGCTAACATGGCTGAGTGGACTTTATGTG  
CTATCTCATTACAGAAAACAGGAGCAATCAGAAAGGAGTCACCTCCTATTT  
GTACCCAGGAATTGCTAACCTACTTGCATCTGAATGATGTCCATCACTT  
CCCTTCATCACCTCCTCTGGGGGCTCTGCAAGGATTTGACTCCTGCATTA  
GTGATCTGTCTCACCTACGTTGTGATTACATGAACCTTACTAATGTGCTA  
TGTGACAACTACCATCTTAAACACAAAACCCCTCTTTTGATTCTGTGGCT  
CCCTCCAGCTACCCCTGCATTTCTCTGTCCCCCTGCCCGTCTCTGCACT  
CACTTTTATTTTACAGCAAACTACTCAAGGGAGTCTCAGTGCTCCTTGG  
CTCCATGTCTCCACCTTTCACTCTCTCCTCAGTTCACCTCTGTCAAGGCTT  
CCGTCTCAAGCTCTTCTTCACTTTTGTCTTAGGGCCGCTGACATCCTCT  
TTCTTGCCAAATTCAGTGGCCAGGTCTCACTTACTCAACTGCTCAGCAT  
TGTTGGGCCCTGGTGGACCACATTCTCCTTCAACCACCTTTTGTGCTCTC  
TCTTCTCTCCAGATGTTTCTCTCTCTCACTGGCTACTCCTCTTTTGTCT  
CCTTTGTAGCTCCATTTCTTCTTCCAACCTCACTGTGCTGGTGTGCCC  
AGTGGCTCAGTTTTAGCTATTCTCTCTTTTCCAGTGGCATTCAATAGATG  
GTATCATGTGACCCATGGCATTATATGCCCTTCTACATGACAGTTACTCCT  
GAATATGAATCTCAGGAAAGATTTGGATTTATTTTAAATTAATTTTTTTA  
AATTTTATTTTAAATAATGAGGTCTCTCTCTGTCTATCCAGGCTGGAGTGT  
AGTATTGAGTGATGTGATTATAGCTCACTGCAGCCTTGAACCATGGGCTC  
AAGTGATCCTCCTGCCTCAGCTTCTGAGTAGCTGGGACTACAGGCATGT  
GCCACCATGCCTGGATGACTTTTTTGTGTGTGTGTGTGTGTGTGGAGACAG  
GGTCTTCTCTATTGCCAGGCTGATCAAACTCCTGGCCTCAAGTGAT

FIG. 3 (39 of 52)

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CCTCTCACCTCAGCCTTCAAAGTGCTGGGATTACAGGTGTGAGACCACTGGGCTAAGATTGAGATTTTGTATTCAATTGACTGTTTGACATCTTCAC  
TTGGACACCTAAGAGGTATCTCAAAATATTAATTAACCTTGGCCAAAATACA  
GAACCTTTTGACCCCTGCCCCACAATACTTGCCCTTCCCCAGACTTCTC  
CAATTTCTGTTAAATATCCCCAGTTACTCAACCCTCAAACCTATGAATGCC  
CTTTGATTTCTTTCTTTCCCTCATCTCTACGTTGACGCCATCAGCTAGT  
TTTGTTCCTTTATGCCCAGAATATAATCCTCACCACCTTCTCTCTATT  
GCCCGAGTATAAGATGTCAGTTTTTCTGCACAGTCCATTGCCCTGACCT  
CCTGAGTGGTTTCTTCCACTTTTGACATTTGTATTCTCTTTCCCCCAG  
GGTCAATTTTTCACAGCAAGAGTGGCATTTTTTTTTTTTTTTTTTTTTG  
AGACGGAGTCTCGCTCTGTGCCCCAGGCCGACTGCGGACTGCAGTGGCG  
CAATCTCGGCTCACTGCAAGCTCCGCCCTCCCGGTTACAGCCATTCTCCT  
GCCTCAGCCTCCCGAGTAGCTGGGAATACAGGCGCCCGCCACCGCGCCG  
GCTAATTTTTTTGTATTTTTAGTAGAGACGGGGTTTACCTTGTAGCCAG  
GATGGTCTCGATCTCCTGACCTCATGATCCACCCGCTCGGCCTCCCAA  
GTGCTGGGATTACAGGCGTGAGCCACCGCGCCCGCCAAGAGTGGCATT  
TTAAAACCATATATTAGATCATTGCTTTTGTGTTTGGGAACCTCCAAGGG  
CTTTGCATCATATATCAAGTTGACACCTCTCTACCCAAGCCTGGCTCTT  
TCCTGCTCCTCTGTCTCTCAGCCCCCTCCACCCATTGTTTCATGCTGCTTC  
AGCCACCATGGCCTTCTTGCCATGCCACATTTGTGCTAAGCCACATCCA  
ATCTCGGGGCTTTGCACTCGCATTTCTCTGCTTGGCATGCTGTACCCC  
AGATCTTTTCATGATTGGCAGCTTCTGTACATTCAGCCACCTGCTCAAGCC  
ACCCCTTTGAGAGGGCTTCCCTGGCCACCTCACCTGAAATAGCACCTCCG  
ATTGCACCCATCCGGTTATTCTCCATCCTGTTCTCTTGGCTGGTGATTTT  
CCATCACTGATGAGGAAATGAACCATGGAATGCTAGGGCTGATGACCAGA  
ACTTTCCCCCACCCTCACATTATTACAGAGGAGGAAATGAGGTCCGAGGT  
AAGATGGGCCCAGGATTTCTACTCCCGCTGGACTGCAGGCACAGCACTG  
ACCTCAGCTGTGCTCACTCTTGCAATTCACCCAACCTTCTATCTCCAAC  
TGCCCCATTTACCAAGAGTGAAATGTTCTCAGAGACGGTGAGCCACCTG  
ACTTGGACAGCAGCCCAGGGCCCCCTGGCACCTGCTTTCTTCTCCTGC  
CATCCTTTCTCTCCAAGACCTACCTTTCCCTGTGATTCTTGCCACATG  
CTGCATTTTCATGGTTTTATGACCTGATTTCTGAGAGGGATTTGAATTTTC  
ATGATTATTTATGTAAGCAAATCATTATGCTTATACAAATGAGAAAAGGA  
GTGCTTCTGGACTTCCCAGGGACAAAATCTTGTCACTTGGCTTGGCTTCA  
TATTGCTAATTAAGGACCAGGATGTGGGTGAGATGTGCTAAAAGCTGAG  
AGGAGGCTCTGGACTCTGACTATGGGCCACACCCCTGGGCAGGCATCAC  
ACTAGTCTTTTAGGTCATCTCAACCCAGCTTCCAGTTGAATCAGATGTT  
TGTGAATAACTCAGCAAGGCTGTATGGGAAATGAAGAATGAGGTGGGGAA  
GAGGCTCTGTCAGAAGACACACTGACTTACCCCTCTACCTCTAACTAGGG  
TGTGTAGCAGCCACCCACCCACCAAGTCTGTCTTCCAGACCACGTATGC  
TTTCTCCACCTTTGCATCTTTTATCTTCTGCCAGCCAGATGCTTGCTG  
ACTCCAGCCCAAGCCTATAGGATAAGCTACAGCCTGTCCCTACAGACTAC  
GCATTGCAGAATCTAAGACATCAAGTCAAGTTTCGGAAGCACTTGCCTTCT  
CCTCTCCAGGTACACAGGCTCTCCTGGAAAGCTGGTAGCAGCTGTGGAGG  
TGTGGTGTGTTACCTGCTGCAGGTGCAGAGAAGTTGACTTCACAGCCCTT  
CAGAAAGACTGCCTTCTTCCAGTTGTATTGTGTACTTGCTTGGGTGTGG  
GGAGGATTCTCAGCTTTCTCACTCAAATTATCAGACCCTTTCCATTAG  
TGGTAGACCATTTCCCTCGTCCAGGCCAAGGGCACATAGTACAGAGAAAT  
AGGGAGTTGTTACCCAGGGAGAGAACTTGGCTCTAAACCTGTAATAGAAA  
GGTCAGTTCTGGTCTGGAGGGTCAATTTTGATCTTTGGCTCAGATCCAGG  
AATTGGAACCAAGGCTTTTGAACATTTTAATGCAGGGGATTAAAAAATG  
ATACGAGTCATTACGAATATATTTGCTTAACATCTAAAGAGATCCCTCA  
AAACACTAGAAAAAATAAGAACAAAAATCTAATAAAACAAAAATTTGTTAA  
ACACATTTACCAAATTTTTTTTTTTGGTAAAAATTCAAATGTCATAAATA  
AAGCTAAAGTTCTCTTGATGACTCGCTCCTCTGCCCTATTCCACTCCAA  
GTAACCACTATTATCAGTCTTGCCAATACCTTCCAGACCTCTCTACCTC  
TATATACCATTAGAAGCACATGGTTTTGTCATTGAGGATGTGCAGTGTGTT  
GTTTTACGTAAATGTTATCACTCTGTTCTTGTTCATAATTTGCCTTTTT  
CTCTCAATGATTTGCTTGGCTATCTTTCTATTTCACTAGCATCTCCTTTC  
TTTTTAACCTACCATTTGTTTATTTAACCTTGCCTCTATCAACAGATATGT

FIG. 3 (40 of 52)

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AGGTTGTTTCTAGTTGA.TTCATTAAGTATTTATAAACAACGCATCAGTA  
 BATGTCCATAAAATTTCTTTACGGAAGATGGCAAGTAGTGGAAATTTGCTGAG  
 CCAAAGAACATGTTTTAAAAAACCCAAAAAACTAGACGCTACCAATTTTC  
 TCTCCAAAATGGCCATACCCACTTACCCATACAGAGATGATTTGGAATCT  
 GGCTTCCCTCACAAAGGTGAGATGCCTTCACAGTTTCATTCTTCTGGCATG  
 TCTTCCCTTTTGTATCTGAGAGAGCTGGCAGAATTGTGTCACTAAATCAA  
 GGATAGAGGGTCAAATGACAGCTCAAGCTCACAGGCACCTCTGCTTTCTT  
 CCCAGACCACCTGCTTTCTGCCCACAGCTCTGTTCCATCTTATAGAATG  
 GTTGCCCACTTGGGTGCTGCTCCGACAGCCATGTCTCTTTGCACTGCA  
 GTTATGAAGCAGACAGAGCTAGGAGAGGGGCTTTGCCAGCCTCTGCCCTA  
 GCTTGGAGAATTTCAAAGAAGGAGGGTATTGAGAGTGAGCTGCCGAAGAC  
 TGGCAGCTCCCTCAACTCAACAGTTGTCTTCCACAAGAAGTCAGATACA  
 TTTTTTTGGGATAAAATATTTAAAAATTATTATTTTATTTCTGAATAATA  
 TATTTACATGATTCAAATACTAACTGTAGGCCAGGCATGGCTGCTTATG  
 CCTGTAATCCTAGCAATTTAGGAGGCCGAGGCGGGAGGATCACTTCAGCC  
 CAGGAGTTCAAGACCAGCCTGGGTAACATAGTGAGACCCTGTATCTACAA  
 AAATTTAAAAACAAAAATTAGTTGGGCATGGTGGCTGATATGGTTTGGCT  
 CTGTGACCCAACTCAAACCTCATGTTGAATTTAATCCTCAATGTTGAGG  
 GAGGGTCTGGTGGGAGGTGATTGGATCATGGGGTGGGTTCTCCCTTGC  
 TGTCTCATGATAGTGAGTGAGTTCTCACAGACCTGGTTATTTGAAAGT  
 GTGTAGCACCTCCCCCTCACTCTCTCACTCTCCTGCTCCGCCATAGTAA  
 GATGTGTGTGTTTCCCTTTGCTTCCGCCATGATTGTAAGTTTCTTGAA  
 CCCTCCAGCTATGCTTCTGTACAGCCTGTAGAATCTGTAATCAGTTAG  
 ACCTCTTTCTTCAATAATTACCCAGTCTCAGGTCATTCTTTATAGCAGT  
 GTGAGAGTGGATGAATATAGTGCCATATGTTTGTATTCCAGCTACCCAG  
 GAGGCTGAGGTAAGAGGATTGCTTGAGCCTGGGAGTTTAAGGCTGCAGTG  
 AGCCATGACTGTACCACTGCTCTCCAGCCTGGGTGACAGCGAGACCTTGT  
 CTCCAAAAAATAAAACCCAACTGTGTAAATGTGTTCAATAAAGTGTCT  
 TTGCTCCACACCTGTCCCTATATATCTTATCTCAGCCTCCGACAACCT  
 ACTTTATTCAATTTCTTATGTATCTTCCAGAATCAAAAAAATAAATAA  
 TACAAGCACAGTGAATGTATTGCCCTTCTTCCCTCCCTTTTGTACAT  
 CAGAGTTAGCATGAATATACGGTCTGCATTTCTTCTTTTTCAGCTA  
 TCAGCATGTTTTGGAGAGGATTTCAATTCGTGCAGACAGCATGTATTAG  
 TCAGTCTTTCATTGCTATAAGGAAATACCTGAGACTGCATAATTTATAA  
 AGAAAAGAGGTTTAATTGGCTCACAGCTTCGCAGGCTGTTCCACAGGAAG  
 CATGGCAGCATCTGCTTCTGGGGAGGCCTTAGGAAGCTTTTACTCATGCA  
 GAAGACAAAGCGGGAGTGATGTCTTATATGGCAGGAGCAGGACTGAGAG  
 AGAGAGAGAGAGAGAGAAAGGATGCCACATACTTTTAAACAACCAGATCT  
 TGTGGGAACCTCTGTACGAGAACAGCACCAAGGGATAGTGCTAAACCAT  
 TCATAAGAACTCCACCCCATGATCCAATCACCCACACCAGGCCCCACC  
 TCCAACATCGGGGATTACAATTTGACATGAGATTTGGGCTGGGACACAGA  
 ACCAAACAATACCAGAGTGCTTTCTCATTCTTTTCTATAGCTGCCTAGTA  
 TTCTATGTCTTTTACTTCAATTTAGGCAGTCTCTTGTGATAGACACTTGG  
 GTTACTTCCAATTTTCTTATTACAAATGATGTGCAATGAATAATTTTGA  
 TCATTTTCCATTTCAATGGGTTATGTCCATCTGTGGGATAAATCTCCAG  
 GAGTGAATTTGCTGGATCAAAGGGGAAGTGCACTTGTGATTTTCATAGTT  
 AGCAATTTTGTCTATAAGGGTCATATCAATTTATAGTCCCACGCGTAA  
 TATTTAACAGTGGGGATTTCCCGACAGTTTGACCAACAAGGTCTGTTGTT  
 AAATTTTGTATTTTGTCAATCTGATGGGAAAATACTAGTATCTCAAAGT  
 GCTTTTAAATTTGACTTTCTTATTACAATGTTAAGCATCATTTTACTCTGC  
 CCAAGATCAAATAGTATTTTCTTTTCTGTGAACAGACTGTTAAGATCCCT  
 TGCCTCTTGTGTTTGTGCTGGATTTTGTCTTTTCTTTTCAAATGTTTTGAGG  
 CAGTTCTTTACATGTGAAACAAGTTATCTCTTTATCTGGGGTGTGAGTTA  
 CAACTACTTTTCTCTGGCTTGTGTTGCGCTTTGACTTTGCTTCTGGTGA  
 TTCCCGCAATCTGAAAGTGTACTTTTTCATCATTCAATCTTATACACC  
 CATGCTCTTGTTCACGCTGGTTCCTCTACCTGAGGGCTTTTCTTTTCTG  
 CTTCTATCTGGGAACATTTTTTTGAGAGAGAGTCTCACTCTCTCGCCAG  
 GCTGGAGTAGTGCAATGGCGCGATCTTAGCTCACTGCAACCTCCACCTCC  
 TGGGTTCAAGCAATTTCTCTGCTCAGCCTCCCAAGTAGCTGGGATTACA  
 CGAGCCCAACCAAGCCAGCTAATTTGTTGATTTATTTATTTATTTT

FIG. 3 (41 of 52)

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TGTAGAGATGGGAGTC. LACTATGTTGCCCAGGCTGGTCTTGAACCTC. J  
GGCTCAAGCGATCCACCCACCTCGGCCACCCAAAGTGCTGGGATTACAGG  
CCTAAGCCACCATGCCCCAGCCCATGTGTGGAAATCTTCTGTTTATCCCTT  
TAGGCTTGATTCTTATGTCTGTTCTCCTCCCTCCTTCTGGATACTCCTCT  
TGTCTTTTATCTTACTCTACTTGTCTATGTTACCTGTTTCTGCTTATAAC  
TAGCTGCTCTCCTATCTGAGGAGGACTTGTGACTGTTCTCATCTCTGT  
ACTCCACAGCTCCTAGTACATAGCGCTTGCTCAACAGATGTTTGGTGCATT  
GATAGATAAATCACTGGTAGCTGTTACTACCAGTCCTGACTCCCTGCAGT  
GCTTCAGCTGATCCTGTTCCAGATGTGCACTGAATATCCTTCTGTTGAAC  
AACAGAAATAAAGGGGATGGGTGAGGAGGATAGTCTTCGGTGGCCAAGGA  
TATTTTTAGGTACTTTGCAGCACTCAGCAATGAGGAGTGGGCTTTAGTCC  
CCCAAGAAGTCTCACAGCCCTGGGTGCTTTACTGTTCACTGTCAAATCC  
AAGACAAGTCAATGATCAGGAAAGACCATTTTTTTTTGTTCAGTGAAGTT  
TATTTTCAAGATCATTGAACAGTATGATATTTGGTAATTTCAATAATATTC  
CCACTTTAAATGATCGGAGCAGATATATTTTCACTCGTAATTAAGGACA  
TGATTTAAAGAGAGCACACCAGTCCAAATTGAAATGATTCCATAGCTATT  
AAAAAACTAGGGTTTTTACAGACAATGATACTTTTTGCCCCCTTTGAAT  
AGATTAGACCAATGAATAAAACAAACAAATAAAATAAATAAATAGGG  
AAGCGGTTGCTCATCAGAATGTGGGAGCGAATGACAGAGGGTTTCTTAGA  
ACCAAATGTGGCCGTGTTCTGTCAAGCGTGCTTTAAGTGAGTAGGAGA  
GGTGAGAGGGCTTGCTCAACAAAAGGGCTGGGGATTGTCCCTGAAGAA  
CCAGAGCTGANTNCATCAGGAGTAACANAGGTAGATAG

>Cont:1941

CCGCGTTGAGGTTCCACGCAGTTCAAATTATGTCCAATTATCAACATTAA  
TGCACATTTTCAATAGAACCTGTTCCGGCTTTTCTTAGGAGGGGGCGGG  
GAGACGTTGTTCTCTGGGAATAAGTGTACGCAGGAGGCTGAGAAGGCTTC  
ATTCCATAGCATTCACTTACCTCCAGCTGTAGAGTGGGCTTATCATCTTT  
CAACAGCGAGGACAGGTACAGATTTTTTCTTTGAGGCCCAAGGCCACAG  
GTATTTTGTCACTTCTTCTCTCTGTACAAAGGACATGGAGAACACC  
ACTGAAGAAAGAAGGGGGTCTTGTGGTTAGGGACACAGCAGTGCAGGGTC  
ACCCCAACCCCTAGGCCCATGAGTAGGATACATGTAATTTGGTAGCCTC  
TGTGGGAACCCACAGTGAGGTTCTTGGCCTAAGACACAGGATAACTTGA  
CTTCTCACAGACAATAGCAGGGTCATTTTGTGATTTAGGGTTTCCCTC  
AAAGGCTGAGGGTTTCTCAGAGCCTCATAGCAGTAGGAACGGAGAATGA  
AAGAGGGTCTACATTTTAAATGCTGAAGGAAGGAAGGAAGGAAGCCATTG  
TGTCACTGGCTGGCAATGTGCCCATCCACAGGAGCGGAACAACTTGATCA  
ATGTGGAAGGAAGGAAGAGGTGAGGCTGTACTTCTGCCAGAAATCAGG  
CACCAGAAGTGTTCAGGAACAGAGAGTAGCCCATGGGAAGAACTGGGA  
GAGGAGAGGCTGAGCTGGGAAAGTGGCTCCAAAGAGAGACACTCATTTTG  
ATCTTCTCAGTCACAGCAGTGTCAATTGGAGGCCCTGGGATCACTCTTA  
CTACCCGATTCCAAAGAAACAGGATTTTCTTGGCCTGGCTGAGAGCAAAT  
AGCTTCCCTCTGAGTGAGGCTGTCTTCAAAGTCAGCAGCCTTAGTTGCC  
CACACTCCTGTGCAGAGGCTTTGGCTACTGTGGCACGATGCCAGGCAGAT  
CACCACAGCTAATGATGGGTTCAACGCACTTGAACTTTTGCCCGTTACA  
GCGGAGAGATATAAGTTCCTGCTGGGCGTAAATTTCCCTACAAGGAAC  
CACCTGGCATTGGGTGGGACGGATGTTGGGGCAAGGGGGGAAGACTGGGG  
AGGGGGATGGACACATTATCGCTCCAGCACTCTTGTTCAGCCTCAACAA  
CAGGAAGAGAGAACCCACAGGCAGTTAGGCCATGTCCATCAAATGACCCC  
ATATTGTGGAAGAATTGACATTGCACTATGCCCAAGAGACTTGGGTGGAC  
ATGGTCTCTGGGAGTGCTTGAGCCGTCTAATTTCTCAGGGTCACACTCCTG  
TTAACAAATGCACTGGCCAGTGCAATCAAATGTGCCATTTCTAGGACCAA  
AGTTTGTATATTCCTTTTTTAATATTTTTTTCACTTGTGTTGATCATTG  
CCTTAAATTAACCTTTCTACTTTGTTTAAACATGGAGAATTAGCAAGCTG  
CCAGGAGGCCAGGCAGGGAACAGGATGTTTCCATTTACCTTGTGCTC  
CATATCCTGTCCCTGGAGGTGGAGAGCTTTCACTTCATATGGACCAGACA  
TCACCAAGCTTTTTTGTCTGTGAGTCCCGAGCGTGCAGTTCACTGATCGT  
ACAGGTGCATCGTGCACATAAGCTTCGTTATCCCATGTGTGGAAGAAGAT  
AGGTTCTGAAATGTGGAGCACATGTTGTTTAGGTATAAAATCAGAAGGGC  
AGGCCTCTGAGGCGAGGTGGCAAAATTTGATTTCTTGGAGGACACCTGA  
GCATATACGGTCAAAGTCTGATGACAACACCAGTAGGGATGAAGCTGGGA

FIG. 3 (42 of 52)

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GTGGGGTGGCTAAGAACTGGACCTGACACTATTAGACATGGGTTCC...  
CTTCAGGTCTATTACTGCTCACTGTGGCCGAGCAACAGAGCTACTTAGGT  
AAAATGGTGTATGGTCATAACACTAGCCACAGGGAGGTTACGAACCTCTG  
GTGACAATGTAAAGTGAAAGGCCCTGAGAAAGAGTGAGGGGAGTTGCAAAAT  
GTCAGTAGCCATCAAGATCTTCTTTAAGAATAGTTTCCACTAAAGAGATG  
ATTGCTTTGGTTTCCAGCCTTCTTTGTTTTGTCTCCCGCTGGGCCTTCT  
ACCTTTAAAGGGCTTTGGCTCTGGGGGAATTGAGTTGGCTGGGGCTTGAT  
GACTTCCAAGAGGACACAAGTGGAGATCTACTGCCTGCTCTTGGCTAACT  
ACCTTCTTCAAAGATGAAGGGAAAGAAGGTGCTCAGGTCAATTCTCCTGGA  
AGGTCTGTGGGCAGGGAACCAGCATCTTCTCAGCTTGTCCATGGCCACA  
ACAACCTGACGCGGCTGCTGAAGCCCTTGCTGTAGTGGTGGTGGGAGAT  
TCGTAGCTGATGCCGCCATCCAGAGGGCAGAGGTCCAGGTCTTGGAAAGG  
AGCACTGCGGAGAGAGCGAGGGAGGGAGCCTGGTGAGGTGGTCTGCCAG  
GAACCATGCTTTGACATCAGAGAGTAGAAAGCTCAGAGAGGAGGAAAGGG  
CTTGAAAGAATCCCGAGCTTCTAAAGATCATCCCTCTCTGGGCCAGGCGT  
GGTGGCTCATGCCTGTAATCCAGCACTTTGGGAAGCCGAGGTGGATGAA  
TCATTTAGGTGAGGACTTCAAAACCAGCCTGGCCAACATGGCGAAACCCC  
TTCTCTACTAAAAATACAAAAATTAGCTGGGTGTGGTGGGGTGACCTGT  
AATCCTAGCTATTGAGGAGCTGAGGAAGGAGAATCGCTTGAACCTCAGGA  
GGTGGAGGATGCAGTAAGCCAAGATTGTACCACTGCACTCCAGCCTGGGC  
AACAGAGTGAGACTCTGTCTCATAAAACAAAACAAAACAAAACAAAACAA  
AATAAAATAAAATAAAATAAAAGATTATCCCTCTCTGAAGCTCAAGGAG  
GTTAAGGGTGTACTCAAGGGGCACACAGCAGGTTAGAGGCAGACTCAAGAT  
TAGAATGTGGGCTTTCTGACACCTTACAGGCTATTCTTTTAGAATAAATC  
CCATTTCTACTTTGTTCATCTTTTGTACATGCCCCACCTACACCATAC  
ATGTATACCTTCTCTATATCTTTTGTATCCCTAATGCTGTCACTATG  
ATTTGCTTTTTCATGCAGATGACCATAACATTTCCATTACCTATGCTC  
ACTCAGCAAGTATTCAATTTTCTACACTGTTCTTTTTTCTTTTTTCA  
TAACACTGTCTCATAGGCATTCTGCAAATCCTGTGAGAGTACTTTTTGTG  
AAATGTTACCACTTTCTCTTATTGAGAGAAGCTCCGTATTAAGGCTTCA  
CTGAGGTTGCCTTAAGGCATGATAATGGTTCAAAGGCTTGAAAGACAGTT  
AAAGAGACCTGTAAGTGACAAAAGAAAGTTGAGCAGGAGAGAATTTCTT  
GCCTGGAGCAGAGCCAAGCTGCTGGAAGAGGCAATGGGGGCAAAGGCCAG  
GCAGACAAGCCAATGGGCTCCTCCACAGCTGCAGCCAACAAGTTATGCC  
AGTCTTAAACCTTCTAAAGAAATATGTTTTTAACAAGATTGAGGACTGGA  
TTATGAGGCTAGGGGAGGCTATCACAACCTGGAATAAAATAAAGCCAGAG  
AAAAGTGGCTGCCTTCCAACCTGCACAACCTGACCTAGCTAGGCTGATGGC  
TGGGCCACCTAGGAAGGCTACTGAGCATCATATAAAACAGAAGGGACAGC  
AGGAATATAACATGGCTCTTTGTAAGGATGAGTCTGAAAAATGACCATT  
GCTGCCCAAATGCCCTTAGCTACAACCTGAAATATTTTCAAACTGGAGGT  
TGCAGGATGCTGGAATCTCAGAGATCATCCAGCTCAGCCCTTTATTTTTTC  
AGATGAGGTCCAAAGCGGGTAAATGACTTGTCAAGGTCAAACAGCAAGT  
GAATGGTTTTCTTCAAGTCTCAATTCATCTTTTGTATATCATCTAT  
GTCTTGTGTTATAAGCTTCACCCCAGGTAGCAAAAACTATTCTACTCA  
AAAGGGGTAGACATATGTTAGTTCTCAAGATCATCTTGGTTTCAGAGT  
TTAACTCAAGTGATTGGCATAGGCTGAATCCATCTCTTAAAGGATAATC  
AAATTTATGTTGAAGACTTGGTTGTCTTCTACTATGAAATGGGAAACAT  
TATCACTACTCCTCCCTGTCAACCACCAAGTGTGGCCACCACCACCAACG  
TTAGTGAGTGACTGTGGTGATATGATGACCAAGTGGCCAGGTGAGCAAGT  
GGTGCAGCCTGTGTCTCACTGGAAGAGGTTAAAGTCTTTCTAAACAAAA  
TACCATGGCATCAAAGTGGCCCAAGTCCCTTCTTTGAGCTTTCCCTGT  
GTTAGAGCCCTTCCCTGGGTTGGGAGTTAAACCCATAGTCTTACCTTCAT  
CTGTTTAAAGGCCATCAGCTTCAAAGAACAAGTCATCCTCATTGCCACTGT  
AATAAAAAACAGGACATGTCTCAATTATGTCTTCTAAACAGGTTTATTTT  
TCCTTCCCTGTGTACAAGACTTGACTGTTTATAAGAACTGCAACAGCC  
TGCCTCTCAAAGCTGCCTGAAACACCTGGCAAGTTTACAGTGATATGCG  
CAGAACAGTCCAGAAGGCAGATTCTAGGCCTGGCAGGTGGGCACCTGGG  
TGCTCCCTGTGGATCTTGAGGCCTAACCTCTAGCCAGCAGAGTCAGCT  
AAAACTGAGCTCTCCCTCTCCCTCCAAGCCACACTTTGCAAAGGGATTC  
CTTGATTTGGGCTTGAATCTTTTCTCCCAATTTGCTCTGCAGGAAG

FIG. 3 (43 of 52)

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CCCTTSCAACACACA TGGATAGCCTCCAGGTCCCAAGGCTGGAGC A  
CTTGTAATGGGAAAGTAGTCTTTAAATCAGATTTACTTGGCACCCCTGTTT  
GCCACTGAAAGAGGCAATTTAGGGGAAAAATCTGGTCTCCAAGCACAGAT  
AACACTCTACTCTTGAAAGAGGAGACCTGCTCATGTTACTGGTCTCAGCG  
TCTCCACTGACCTGTAATAAGCCATCATTTCACTGGCGAGCTCAGGTACT  
TCTGCCATGGCTGCTTCAGACACCTGTGTAAAAAGGAGAAAAAGAGTGAC  
TTCCCATGACGGCTACGTTTCATGTGTGATTTCTCTCAGCATCCAGTGCA  
TGGCAGTCATGCAAAGAAATGATCTCTGAGTAAATGAATGAATGTGTGAA  
AGAGAAGTCCTTTGGGTCTAGAGAAAAGCATTGCTAAACCAAACCCCAA  
CTAGCAATGTATTGGCTAGGAGAGCTGGAGCAGAGGCTTTGACACTAACC  
TTTAGGGTGTCTAGCTGTTAGATAAGCAGTATCCATTCCCAGAATATTTCC  
CGAGTCATAAGCATTATATTACACCTGGCATTTTTGCAAAAAGCTGAGAG  
AGGGAGGAGAGAGGGAAGGAGAGGAGAGACAGAGAAAGAAAGAGAGAG  
AGAGAGAGAGATGTCATACACAAAGAGGCGAGAGAGACAGAGAGACTCC  
CTTAGCACCTAGTTGTAAAGGAAGATTAAAGTCATACTTGAGCAATGAAGA  
TTGGCTGAAGAGAATCCCAGAGCAGCCTGTTGTGCCTTGTGCCTCGAAGA  
GGTTTGGTATCTGCCAGTTTCTCCCTCGCTGTTTTTATAGCTTTCAAAG  
CAGAAGTAGGAGGCTGAGAAATTTCTCTGTTGAATACCTGATTTACAAT  
CAAGTTAAAGGAAAGGGGAAAGAGTATTGGTGAAGCTTCTTAGGGGAG  
GGGACTAATAAAGTGAATAATTCTCTGGTTCATGGAAGGGCAAGGAGTA  
GCAAACTATGACACATTTTGCAAATGTATCACCATGCAAATATGCATTGT  
TTTCTGTGACAAATCGTTGTGTCAGTTGATGTCCACATTAAAATACTGGATTT  
TCCACGTTAGAAGAATGTTTAAATTTAGTATATGTGGGACAAAGTGGAA  
GACACACAGATTTATACATGCACATACTTTTCTTCATTCACTTCTTTGTA  
CTTAAGTTTAGGAATCTTCCCACTTACAGATGGATAAATGGGTACAATGA  
AGGGCCAATAGCCCTCCCTGTCTGTATTGAGGGTGTGGGTCTCTACCTTG  
GGTGTCTTCTCTGCCTCGGGAGCTCTCTGTCAATTGCAGGAGCCTCTGA  
GGAGAAAATTGACCTTTCTTGGCTGGGGCAGAGAACATACGGTATGCAGG  
GTTCAGGCTCCTGACGGAGTTGGGGCAACCTGGAGATAAGCTCACACAA  
CCCTGCAAGACCAGGTGCTGTTACCCTAGCCAATCTCATGGATGAACCAG  
ATCAATGCCAGATGAGCTCTGCCTAAAATGATTTTTTGGTGAAGCTCTGAA  
AAGTGAATATTTGTTTCTGTAGAATATCCATCTGAGACTCTATCTCTTG  
GTAATACCAAGAGTTATCAGTTTCTCTTTAACCGAGACACCAGCAAAGTG  
CCTGCTCCAGGGTAATGCCAGGGGAGCCCTCCATTGTAGAATGAATGA  
GAGTCCAGGTTATGAACAGTGCCTGGAGTGTAGGAACACCCTCCTTTGCC  
TCTTGTGACAGGTCTGCATCATAACACTTTTTTTTTTTTTTGTAGACAGAG  
TCTCACTCTGTCCGCCAGGCTGGAGTGCAGTGGCAGCATCTCGGCCCCCT  
GCAAGTTCCGCTCCCGGGTTCACACCATTCTCCTGCCTCAGCCTCCCCA  
GCAGCTGGGACTACAGGCACCTGCCGCCACGCCCGGCTAATTTTTGTAT  
TTTTAGTAGAGACAGGTTTACCATGTTAGCCAGGATGGTCTCGATCTC  
CTGACCTTGTGATCTGCCCGCTCGGCCTCCCAAAGTGTGGGATTACAG  
GCGTGAGCCACCGTGTCCAGCCTGTAACACTTCTTATAGCACTGAGTTGA  
AACCTTGCTCCTCCTGGTTCTCCAGGAACTGAAATCTTTTGTAGCCAA  
GTCTAGCACAGTGCCTGGCATGTACATTCAAGTGGTAGAGTTGCTGCTT  
GAATGGGTGAATGGGAATTTGACAGCATTTTTATTCAAATTAGTATGTGC  
CAGGTATCGTGCTCGCTCTGCATTATCCAAGGGAGTGAGCCTCTGTGCAA  
GTATTTGAGACACGAGGGAATAGGTTCTACTGTGGGAAAAAGAGCATT  
CATGGACTTGCTCTCAAGCAGCCTTCTGATTTTTAATTTGGCTCCCAGT  
ATCTTGATATCAGGAGTCAGTCACAAGAACTCCATCTTTAGTAAGTTATA  
TTTTCCACAGGAAATCTAAAAGCTGTTCAACATGTTAGTTTCTGTGAAT  
TTGATAAGCCATAATCCATTCTTAACACTGAGCCCTCCTGAAATTTGGTG  
TCTGGTCTCGAGATAGCTAAAAGCCCTGTCTGGGTGGCCTAGGGACTCC  
TCTGTTTTGCCTCCACAGGATCCACTTTGCAAATTAACCACTGGTTCTCC  
CGTTGTAGGAACTGCCACCTTCTCAGAGCCTGTCTTTCTTCTTCTTCTT  
CTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTT  
CTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTT  
TCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCT  
CTCCCTCCCTCCCTCTCTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTT  
CTTCTCTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCT  
CTCCCTCTCTCTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCT

FIG. 3 (44 of 52)

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TCTACCTTTATCCCCCAGCTGGAGTGCAGTGGTACAATCATGCATTCA  
 TGCATGATCACAGCAGCCTCAAACCCCTCCTCAGAGTCTTTATGCGGCAA  
 CCAGCAGGGTCTGGAGGGTGGTGGCTCTGTGAACCTCTCCTGACAGAACA  
 CAGAGATGTCTTTGGTCTGTTGATGTGATTACAAGCTGAACGAAGGAAGA  
 TCAAAGCCAGTGACAGGAAGGAGATATGCAAGGGACCCGAGCATCAGCT  
 CTGAGTTAGTCCATTCTGCTTCTGGGACTTGGGATACAGGTCAGAAACCT  
 TGAGCTTCTACTTCTCCATCTTCCAATTGTAGCATCCAGGACCTCAGAAT  
 CTGCCAGCTAAGAGGAGCCCTAATGATTGTCTGGTGGGATATGGTGGGAC  
 CACAGAGATGAAGACATGAATAGCTATTTGAATGTGAACAGCAGACGAAG  
 AAATCAAGGCTAGGAGGGTGGAAAGTGAATCATCCAATAGCACAGTGTGGT  
 TGAAGCAGCACTAGTATCCAGGTTGCATGAGCCCCGTATGCTTTCGCTCG  
 AGGGAAATTTTGGAGCCATGGGGCAATGCCCCCTGACGTAACAGTCTCCA  
 CAGTTCTGCCATGTCTCATCTTGGCCCTGTAACTGGACCCAAATCTGCT  
 ACCATCCCATCCATCTCAGGAAGTGAACCTCTTATGTCAAATAGGTTGT  
 GCAACGTATGTATCAGATCCTGTCTTCCCAAGGAGACCGCTCAGGCCACA  
 GCACTTCTTCCGATCCCCAATGAGCAGAAAATATCTCGCTATAAACATA  
 GTTGGCACTAAGGGAGGGAGTGGAAAGTGAATGATGATGTAGATGGTGT  
 GTAGCCCCAAGGAAGTGGAAACAGCAGAGATGGGGAGCTGGAAATGCCAG  
 GATGCTCCAGCTTTTGGGGAATTATTAGCTCTTGAGTCACTAAAGCCTT  
 TCTCAGCTGCAAGTTCCTTACCTGTGAGGTCATTCTTCCAAGACAG  
 GAGACTGACATTTATTCAAAGCAGCAAGTGGCCGTGATACCATCTTGTGTC  
 TAATCATGGGCTTCGCAGCCAGTTATCAAGGTTGATCTCATCTCATTGGT  
 CTTCAATCATTTTGAACAAGAAGACAAGCAAAATAATCATGGGTTAGTTC  
 TTATATTATTGTGTGATGATGATGCTGTTCTTTGTAGTGAGCTG  
 TCCCTTCTTGTTCACCTCTTGGTTAGAACAGAACTAAGCAATCTGCCC  
 CCAACATTTTCCCAATTTCCCATCTCATTCTTGGCACTGGCTTCCTAAT  
 ATTTGTTCTTATGAGTCATTTTCTTGATCATTTCCATGAGTCCCTCTGG  
 GATCTTAAAGTATGAAAAATGTTGTGTGTACCCACACCTGTCTTTGTGGA  
 TATTTCTCTCTTCCCTTCTGCTTCTGGGATTATTTGGGAATGGGCACT  
 ATGATTTTATCATATCGCTTCCACTTCTTTATGGCATCATCTCCAATG  
 GGCTTCTTCTCCCTCTTGGATCCAGGTTCTCAGATTGGGGACATGCAGAG  
 TCCAAGGAACATTCCATTCTCCTCCCTGGTCTAGAACAAGGAGGGCTTAG  
 ATATATGAGCAGGTGGCTGGGGCTGGCGAGCTATGTAGTCTCCAATGGCT  
 TTTCCCTGATGTCGGAGTTGTTATGTGAGTCTGGGAGACCAATAAGACC  
 TTGTCTTCTTTGGATCCATCAGAAAAAGCCCCCTGGGTGGGTAAAGATGG  
 ATGGCAGGGCTCTCCTACTCTATGTCTTTCTCACACCTAGTGGGTATAA  
 GAGAGGGGACCACAAACAGAGGGGGCTCTGGTACCACTTATCCAGGGTCT  
 GGAAACATTTTCTGTAAAGGGCCAGATAATAAATGTTTCAGGTACAACCTA  
 CTCAACCTTGCATCATTTTCAAGAAAGCAGTCAGATAATACATAAATGAAT  
 GGGTGTGGCTGGACTTGTCTTGGGTCCCTGTCTTATATCATTTGTATTA  
 TATCATTTTCTTACATACAAATTTAGAAGCAATACTTAAAAAAAAAAAA  
 GCCGTCCTTTATTGAGCACCTACTAAGTGCCAGGTACCTTTTTTCCCTC  
 ATTATCTTATTAACCTTTCATAATAACCTTTAAAGTAGATAAATTTGAAC  
 CATTTGACCTATGCAGAACTGAGGTTGAGACAATAAATTATTTAAGACC  
 GCACAAACAGTAAATGCTGGAACTACGACTCAAATATGGGTAACTGAAC  
 CAAAACCAGATCTTTATTTCTCACTTTAATTGTTACATATGTTTATTGC  
 CTCATCTCCTGTCCACATGGTGGCCATCGGCAGACTCCTTTCTCATTCTC  
 AGTGATTGAGTGACATTCTAAACTACATTGGCCTGGCAGATTACCTCTG  
 TCCCCATAATGTTTCCACATTGTCTTTTAGGATTGAGATCCTCTCTGTT  
 CCCTTGTCTTCCCTCCTTTCTTCTTGGCGGTGACGTGCTGTGTGAATT  
 TGTTTCTTTCTCCTCTCAGGGTAGTACTGGGACTTTCCAAATCAGGGTTT  
 TTAGTGATCTCTTCCCTTTCTGAGTTTCTCCTTATTCCCATTCAT  
 TTCTCATCTATAAGTGGCAGCTTTGTTGCTGGAGGATTTCTTTGTCTT  
 TTATTCTTCTTAAAGACTTTGTGCATAACTGTCAAAGCAATCCCTTGAAG  
 GTATCTGTCTTGAATTTGTGTCTTATGATGCTGAAAAATACTCTCTTC  
 CTAAGCTATTATAAATGCT  
 >Cont1942  
 GGCTAGCTGCAACTCTTGAATACAAACACATTTCAGACATGCACACACTTT  
 CTGGCTCCCCAAAAGAAAAAATCAATTTATAAATCTGATCCT  
 TTGCTTATTTCCAAACTCCATGAAAATTGTACATTGTCCAAGCAACAT

FIG. 3 (45 of 52)

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TTCTTAATATTTCTCTT. TCTCTCATATCCATTTTCCTTACTGCTGTC. J  
CACSTATCTCTTCCAAACTCCCTGTTAAATCCCTGCCCCAGCGAACTTT  
TATTCATTTTGTGGAATGGAGGCTGCACTGATTTAAATTAATAAAAAA  
AAAAATCCCTACTCCATGTCCAGATCCCTAGTTGTTTTTTGTTTTTTG  
TTTTCTGAGACAGGGTCTTGTGCTTCCATGCTGGAGTGCAGTGGCATG  
ATCATGGCTCACTGCAGCCTCAACCTCCTGGGCTCAAGTAATTCTCTTGC  
CTCAGCCTCCCCAGTAGCTGGGAGTTTCAAGTATGTGCTACCATGCCTAGC  
TAATTTTTTTCTTTTATTTGTAGAGACACGGTCTTGCCAGGTTGCCAG  
GCTGGTCTAGAACCCTGGGCGGACGTGATCCGCCTGCCTCGGCCTCCCA  
AAGTGCTGGGATTACAGGCGTGAGCCACTGCTCCCGGCCTTGGGTGCAAA  
TTTGAGCTTTCTCACTTATTAGTGTAAGACATACAGCTAATTTCTAAATC  
TTCCAAACCTCAGATTTTTTCATCCATGAAGTGAGGATTATTATAGAGCTC  
ACTAATAACATGGCTTCAAAAATATATAATGCCAAATTGAGATCAAAAT  
AATAAATCTATATTACATGGGAGATCTTAATGTACCTCTTATATTATTGA  
TAGACTAAGATGATCAAAAAATAGAAAGAGAGCAGTAAGGAGAGCAAGC  
ATTTAATCAATAGGACCAATACATTTTAATCAATAGGATCCTCAGGAATA  
TATACAGAATACCAAACCTAACAACCTGCAGAAAACATGCCAAACATTTAG  
GTACAGACATTGTTGGAAAATGCAATCTTGAAACGAGTGGACTGACATTC  
AGAAGATATTAATAAGAGCACTAATGATGGGGATTGCAACCATGTCTTTA  
CTGACTTCCAGAAGCTTCTTACAGTAACATGAAATCACATAATTTCTTC  
CACTTTCCTTACTGTTTCTTGTCTGGGCTCTGTCTGCTTACTGTCTAAT  
ATCTTGGCCCTTAAAGTTGCTAATCTTCCAAACCTCATTCTGTGACT  
GGGCGCTGGTCTTGTTCATGGGCCTTGAAATACTGACTGTACACTTA  
TCTGGAGCATCCAGTGCCTACCACCTGACCCAGATTCTCTATTGCGCTCC  
TCCCTCTCCACCTATTGGAATTTGCTCATACCCGTGTGAGACCCCTCCC  
TTTCCCCCATCTGAATTTTATCAAGACAACGCACTGCCATACTCCCTC  
GTACCTGCTCTGGGCATCAGACTGAATGTTTGTTCATTGAGGATCTG  
CAGCTGCATCAGTTTCCCCAGCACCGTCCAACCCCTTGAGCATGGCTAGT  
CCTAAAGCAGAGAATTAGCCTTTCTATCCCTGCTGCTATACATGCTGGGA  
CAAATAATAAGAAATGACAGCATTTTATGATAATGCAGGCTGCAGGAGGC  
AGGAGGCAGGAATCAAATTCGTGCTTATCAAATAGTGCTCCAATTCTTTG  
AATATTGACTATAGAATATGTATGGATCTATGCTCAGGTGGGTTCCTT  
ATTACTCACTCCACTGAGGCCAGGTTGTGGGATTAGCTGTCCAAGAGGGA  
GTTTCAGTCTCACAGCATAGGGTCATTCTGAGAATTACTGGCCCACTT  
GTGTGGAGACCTCCAGAGAACAAGATCTGGGTTGGTGCCATGTACTTCA  
GGAGGAGAGAAGTGGCAGGATGCCAGCCCCACAATCAGAGGGGAAGGGG  
CAGAGCCACATGTATGAAGATCCTCTCCCCAGTACGTGCCAATCACAGG  
CTTCTAGCTTTTGGGCCAAGGAAACAATGTGGGAAGCAAAAAAGGACAA  
TTTTCTCTCTCTTTGTCATGAAGACTGAGCAGTTTACCAGATTCCCAGG  
GAAACACCTTCCACTCTGGGTTGAATGTGAGTGAGAGACATTAGCTGG  
AACACTAGAAAACTATTTCTTGAGCCACTCACCTTTAGCCCTAGAAAGT  
GTTGGATTTGTCTTTCATCTTTGCCACAGTAGAGACTGCTGATAGCATCA  
GAACTTGGGCTCTGGAATTAGACAGATATGGGTACAAATCTGAGCTCTCT  
CACTTATTAGTGTGGGATGTAGAGCACTTTTAAATCCTTCCAAACCTC  
AGACTTCTCATGCATGATGTGAGGATTGTAATAGGGCCACCTAATAGGG  
GTTTTTGAGAATTAAAAAAGTTATTCAATGACAGCATTTAGCAAGATGC  
CTGACCATTGAGAAAAATAACAAATTGTTTATTATTATTGTTATTATTAA  
CATCTTCTGACCTTCTGACTGGGGGCATCGTATCATCAGAAATACTT  
AGGATGGGATGGATTCTGTCATGGGCTGAGTCAAGGGTGCAATAATGGAG  
GAGTGAAGAAGGAAGAAATGGAGGCAGAAATCCCAGGAGCCCAGCATGG  
TACAAGGCTGAGCTAGTGTGTCAGAGCCTCCTTGAACAGCCACAGAGCT  
TGTCATCTGGCCCTGGGAGGAACCTCTTCTAGCTGGCAGGACCAGCCACAA  
CAGTGGCCAGGGGATTTCCCAGGGCGTGGGCTCCTAGGAGTTTCAATTTGA  
CCAAGCCTGCCTGGAGAGGGGTTATAACAGGGATCCTTCCCTACTGGCAG  
GTGATTTACCCCTCGGTGAGAAGCTCAGGCATTTGTTTGATGGAAGGTGG  
AAGGCCCTGTGCTGGGCCAGTGACTATCAGGGATGGGCGGGTGGCTGGAA  
AATAGCAAAATAAGACAATATGATAACACAGTTAACCACCACACTATGTGA  
AGCTACAATATGGGTATCTGTAATAGACAATTCCAATGTAGAGAATAATT  
CTAAGGTGTCTTCTCCCCGCAATGCCATAAGCACACGGCCTCTGCCTG  
GGTTCTCACTGTGGAATGTCTCTCTGCTCTCTCATGCCAGAGAGTGG

FIG. 3 (46 of 52)

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GAAGTACTGCTACTTT. .CACCGGCTTTCTGTGTCATCTCCCTGCAGC...  
CCTCAGCCCCCTCTGCACAGGGAGGTTTCTCTCTGCTGCTGCAGTGCTT  
TGTACTTGTAGTGGTACCTGCACACAGGTATTGGTGTCTTGTCTCACC  
ACCTTACATCACTGTAAGCTCCCCAGGAGCAGGCTTCTGTTTGACTCAC  
CTGTGATCTCCACCTCCACCTGTAGTGCCTCAAGCATTGAGGACAAAT  
CACTGGCTGCCCTTAACCCAGAAATGCTGCCGAGACAGGAGGCCATGGC  
CCAAGTTCTGGAATGGGGTATTACTATGTGACGACAAAGGCCTTTGCAC  
AAATGAAGGCTTTAAAAATGCAGTCCTAGTCAGGTGGAGGAGGGCTTATA  
GGATTCCCAGGAATCTGGATCATTCTCTTGAGAGCTTTCCCTTGTCTCTG  
TTAAAACTCACATCCTACGGCCCCAAATAACAACAAAAATGGATGTAAAT  
TCTTGAAATAACTTGTGGATGGGGGAACAAGGCCACCCCCAGATCTGC  
CAGAAGCTTCAGGTGAGGGTCCCAAATGCCAAAAAGTCTGGTATCAGAGA  
GGATGGCCAGTGACCTGGGGACACATGCCCTTGTGTGTCACTCAAGGA  
GCAGCAGCTCGGCCCGCACAGTGACCAGGACCTGGCTTCCCACGCTG  
GGCAGGAGCTGGTGTCTGATGAAGGGAATGCCTGGCAGCAGTGTCTGTCT  
GTCTCTCGTGTGAGCTTACCTGGCTTGTGTGGAAGAGGCCACTCGCAT  
TTCTCAATTTTTTATATTTTTTAAATTTTTTAAATTTTTTATTTTATTTT  
TATTTTATTTATTTATTTATTTTAAATTTTTTAAATTTTTTAAATTA  
TGCTTTAAGTTTTAGGGTACATGTGCACATTGTGCAGGTAGTTACATAC  
GCATACATGCGCCATGCTGGTGGCTGCACCCACTAACTCGTCATCTAGC  
ATTAGGTATATCTCCAGTGCTATCCCTCCCCCTCCCCCACCACAA  
CAGTCCCCAGAATGTGATGTTCCCTTCTGTGTCCATGTGATCTCATTG  
AATTTCTTTAAAGGTGGAATCTCTCAGTGGGGTCTAATCTGTTGAGAAAT  
ATCAAAAGAGTATCCTTGGGAATGACTGGAATTCAGAGTCATCTGGTAA  
TCCTCATAAAACACTCCTGGATGTCTCTCAGCACATCTCCACCTTGAA  
CGCAGGAGGCTGGTTCAAATGGAGGAGCATCGCTCTACTGCACTTTTTTT  
TTTTTTTGGCCTAAAGTGCAAAAGGGGATACGTTTCATGTAAATAAATCA  
ACTGCAAAATCGCTAGTTATGCTGAGCCCTGTCCCGTGTGTGGACACAAA  
GGAACCAAGGCTTTTCTCCCCGCCAACACACACATAACACACACACAA  
AATCATAAAAACATACATACCCCCAACACATAACACACACACACACAC  
ACAAAATATATACACACACACACACCAAAACATGCCACAAACCTGTGTC  
CAGAGATAGATCCTACTGGTGGGTTTGTGGTCTCGCTGACTTCAAGAATG  
AAGCCGTGGACCTTCGCAGTGAGTGTTACAGCTCTTAAAGATGGCATGGA  
TCCAAAGAGTACCCAGTAGCAACGTTTACTGTGAAGAGCAAAAGGACAAA  
GCTTCCACAACCCAGGAGGGGACCCAGCAGGGTTGCTGGTTGGGGTGGC  
CAGCTTTTACTTCTTTTGGCCCCCTCCCATGTTCTGTTTCCATCCTATCA  
GAGTGGCCCTTTTTTCAATCCTCCCTGTGATTGGCTACTTTTAGAATCCTG  
CTGATTGGTGCATTTTACAGAGTGCTGATTGGTGGCTTTTACAATCCCT  
TGTAAGACAGAAAAGTTCTGATTGGTGTGTTTTACAATCCTCTTGTAAG  
ACAGAAAAGTTCCCAAGTCCCCACTGGACCCAGGAAGTCCACGTGGCCT  
CACCTTTCAACTCCATAATGGCATGAAAATACATATGTTGTACAAAACAT  
ACATACACAAAGTATACATGCATCTCCCCAAATATACATACACAGAA  
ACATACACACAGGAACCTCAGCTACCTGTCAAAGTCTGCATGGTGATTGC  
CTCTGCAGTGAGTAGTTAGAAAAGTGAATTTGTTTTTCAATAAATTGGAG  
TCCTTAAAAATCGTTGTAAGATAGAAAATTTTTTAAAGTATATAAAATAA  
AATATGTATGTCTTTGGTCTAGCATTTACACATGTAGGAATTTATCCTA  
GTGGAGTAATCAATGATATATGCAAAGATTTGGACAAGCATATTAAGCAC  
AGAATTATGTATGCATATGTGTGTATATATATATATCTCATACATA  
TAATAATGTAAAAGTGAATAAATCAGATGTTCAAAATTGAGGATTAGT  
TAGACTATGATCTGTCCATATGTGACATACAAGTTAGCTGCCCTTATTC  
TCTCGAGCTTCAACCTCCTATAAACAGTGTCCTTGTATATCAGTATTGG  
TACAGATAATCGAACTTATTGAGGTTTTACATGGGGCAATAAAGGCAAGA  
GTTTATGAATACTCCATACTACACTAGGTAGCACCCCTATTAAAGACAA  
ACTCTTCTCTCATTTCCCTTCCCTTCCGGAACCACTTGGTTGAATCTC  
TACAAGTCTCTATTGCAACTGCCTCAACATGGCACCCCTCCCTGCATCTCC  
ATCTTCCCTGTCTGAGAGCAATGGCCTGCTGCCCCCACTCACATCCT  
CATTCAATCCAGAAGTGAGCACCACAGAAGTGCTTACAGTTACCCCAACC  
ACCTTCTTAGAAGATAAGTTAGTGTGTTTTGTTTTGACTTTTTAAATTTTTA  
CTTCTCTTTTCTTCACAATCTCATCCCATCCCAAGAGGTTTATCAAGA  
AGTTCTCTAAAGATATGTGTCTCCTTATGGAATTTAACAGAAATCAGGGA

FIG. 3 (47 of 52)

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...GATTCAGCCATK AGGGAATAACATTTTTCCAGGTCTTTAGAC  
ATAATGGAATACCTTGACGTAATTAGATACACTATTGTAGAAAAGTATTG  
ATGAAATGGAACGATGTTTGAGATATCATATTGAGTAGAAAAGGCAAGAT  
ACATTAAGTAGGAAATGTATCTTACAAAATAATTTGTGAGACACACTCCT  
ATATTTGTATGTTATATAAATGCGTATGTGAAGAAAGGCTAGAGGATGAG  
ACCCACAGTCTTCGGTGAAGTTTAAGAGATGATGCTGCAGCATGCTCAGAA  
AGGCTTGGTATAGTTTTTTCCAGTAATTAAGGACTGATCTTAGGTAAATT  
GTCCATCCTCTCTAAACTGCACCACCTTTGTCTGTAAAACAGGAAGGAT  
GGTATTTACCCCCAGGGTCATCAAAGGATTTGGTTGGAGAAAAATAAATA  
AATGGGCTGAGCCAGACCTGGCACAGTGAGAGCACAGTGGTTGACTATT  
GTGCTGGCCTGTTGTTCTGTGTTATTGACATGCTGCTGGTGGTGGTCCA  
GAAGCTATTACCTTAATTGGTTATGTGGATTTCCCTCATACTGAGCAGC  
TGTGTGTGGTGTGTTAAAACATAGCCATACACAGTAACTGACAAGGGCAA  
ATGTGATGGAATAATGCAAGGAAGTGCAGATAAATAGCTAATGGGCTGTA  
GAAGGAAGCTAGTCTTGGAGGGCTTGATCAAGGAAGGTCTTTTGCATG  
TCACCTTTGAAGAAGAGGGGACATAGAAGAGGTATAGTGCATCCCGGAGT  
GTACCTGGAAGGGAACATGAAAAGAGGACATTTTTCTCTGGGACATGGGG  
ACTCCACTTGACATGAACCTCTGGAATTGGGGCAAAGAACCATCATGAGAAC  
AAGGGCTTCCTTGAACCTCCAGGCTCATTGGCTGATCTAAACCCTGTGT  
CCCCTCTTTCCTTCACTCTCCTCTGTTTTCTATACCTGTATTATTGGACT  
GGACTGGAAGCCACCTGATCTATACAAGTACCTTGAATGTGTTGAATA  
GGTGTGGCACAGTCTTAGCAGAGTGGCACTACCCCCACAGGAATTTGTT  
TATACCTTTGGCATGGAATAATAGCAGGAAATGAGTGATCACTGATAACTG  
AGGATGCTATTTATTATTGGCCAAAGGAATACTTGTGTTGTATTTGCATA  
ACCACTCACAACTGTTGATTACAAATGAGTACCAGACCTAGCTCCTTCA  
AGTAAAGGATCTTGAGAACTGAAGGCAAACAGAGCTCCAGGAGTCCAAGA  
CAGAGCCACAGACCAGGATCCCTGGCCAGGTAGGTGGTCTCTCTGC  
ACTGGCTTTCAAGGCCAACAGGATGGATGGGAAGTAGAGTAGCATCTGG  
CCATCTAGACCCTTGCTTTTTATCCCCACTGGAAGCACATCTGAATTTCT  
AAATATGATCTCTGAGACCTGCCAGAACACCTTGCTCTCAGCCCCAGTA  
GCAGCCTGCTCTCTCCAGGAGGGCTTCCACTAACAAAGTAGGGCATTGCT  
GGAGGGCCAGGCAGACACTAGCTTAGGAAATCCACCAACCCTGGAAATGC  
TAGTCCCTTCTCTGAAGGCTCAGAAGACTGACTTTAGAGTCTAGAAAATA  
TTGGTCTTGGAACAGATTTTGAGTGCAAAGAGATGGACTTCAGATGGC  
CAGATGCATGCTCTTTTAGGGAATCTGTGAAAGCTCCCTGCATTTATC  
TTAATACAGGCAGCAGATTTTATGAGTACCCCCGAGGGATGGCCCCAGGT  
CCTCCAGCCTGTGAGCATCCTTCTGTCTTCCAGCAGCACCACAGTATCTT  
TATATGCTTTGGATACCTACGTTTCTGCCAGACATCTCTTGCTCTGATG  
TTCTGGCTGCCAAATCTCTGTCAAGCGCCTCCAATTTTTTGTGTCTCTT  
GATTTACCCCAACATGACAAAGGCAGTTGTGCTTCATGTATTAGGGATA  
CTGCCAAACCACAAACAGGTTAAAATCAAATAGCAGATATCCCTGTTCT  
AAAGACCCATCAGCTCTACCCACCTGCTCCTGCTCACCCTCCTTATTGTT  
GAGTCTTGAAGCCCTTCTTGTCAATTTTTATTGTCATGAACAATTTA  
GTTCCCTTTGTCTCACTCCTAAACCTTTCTCAAAGGATTGGATTTGTACA  
CAAACCTGCCTATCTCTGCAATCTTAGAAGTGATATGATTCTGAACAAATC  
ACTTAACTTTTGATTTTTATTGGTAAGATGGGAATACCAATTTTTGCTC  
CACTTCTGTCTATGTTGGCCTGGGCTGATGTTGAAAGCTCTCGGTCAAC  
TGAGATAGGGTGTGCAGAAATTTATATATATAAATATATCTCCTCCAACCC  
CTCCAATGAAGCAAGTCACGTGAGTCAATCCTACCCTAAGATATTAGGG  
ATTGAGCCTCCTGGGACATTTGGTGGCTTAGGTTTTCATGAAAAGAGGTT  
GCAGAGCAACTGCTTTTTGTTAGGCAAAGATTAGGCTACTGCAGAGACTC  
AGCAAACCTCTATAGAAGGTGTCAGATGGTAAGTATTTAGGCTTTGCTT  
GCCAGATGATCTCTCAACTAGTTAACCATGCTATTGTAGCCTCGAAGCAG  
CCAGAGACGATCTGTAAACAAGAGCATGTAGTGTGGCATAAATATAGTA  
CCGCG  
>Contig43  
GCAATAAGTCTATTTACTGTAAAGTTAATCAAATTTACATTTTCAGAACAC  
TTAATCTGCAAGAGTCTTTTCCAAGACCCTATACCTAATTTTGTGTTTAC  
AATTTTATATTTGTTTTCTTAAAGAAGACCACCAATATAAACTATATCCA  
GCCTTCATGATAAGTACATAAGAACTATGCAATAAGGGGGAAAAA

FIG. 3 (48 of 52)

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CAAAGAAAAATACCTAC TACTAATGGTTCACCTCTGAATAGCACAT...  
TCATAATGATACAAGCACTCATTACTAGTCTAGGAAAATGAAGATATAAT  
TGCAATTAGGAAGATCAAGAGGTAGGAAATGTGGATGTGTGGTATAGAC  
TAGGGCAGGACAAAGAACCTAAATCCTCATTCTTCTAAAGATAATTGTTAA  
TACGTAAAACTCAAATTCAGAAGTAACAGTAAAAGCGGTCAATTAAGAA  
ACAAGCACTAAACACCAGATAGGAAGCGAGAGATGGGGGAAGAGGGCAAG  
AATCTGATTATTTTTTGCAACAAATTTTGTAACCATTGTGACTGTTTAC  
ATGTAGAACTTGGATCTTTTTTAAAAAACACAAAATAATAACTATTAT  
TTTTTAACCTGGATTTTTTGAAAAAGAAGATAAAAGTCTCATTTTAGTAATT  
AAAACCTCATTCCAGGTTAGTCCACTCAAACTTATATTCGAAAATTAAAA  
CTTTGGGAGGCTGAGGCAGGCAGATCACCTGAGGTTGGGAGTTCGAGACC  
AGCCTGACCAACACGGAGAAAACCCCGTCTCTACTAAAAATACAAAATTAG  
CTGGGCGTTGTGCATGCCTGTAATCCAGCTACTCGGGAGGCTGAGGCAG  
GAGAATTGCTTGAACCCGGGAGGCAGAGGTTGCAGTGAGCCGAGATCACA  
CCATTGCACTCCAGCCTGGGCAACAAGAGTGAACTCCATCTCAAAAAAA  
AAAAAAAAAAAAAATTAAACCTCTGGAAGTTGAGTTTGCAGATATTCA  
TATGCTCATTTTTAACTTGTATGTTTGGAATGTGATGAGAAATTGA  
GGTTGGGGGATGAGAAAAAAGAAAAACATCAACCCACAGCCCATTCAA  
TTTTACGCCCCGACCCACAGCTCCGGGAAGGGCAGCAGGTCCATCCTTCA  
CTCTTTCTTCACTCTTTCCCTCCTTCTGGCTCTTCCACTCTAAGTTG  
GAGCCCAAGAAGAGGCACTGGGAAATGGAAGTCTTTTGTACGTGGTAC  
TTGCCGGGAAGCTGCCATGAAGACCTGGCCCCACGGTGGGAGGGAATG  
CCCAGCTGAGGCCTCGTGCCCATGCTAGGATAGACTCGTCCAGACATGTC  
AGGTGGTCTGACAGGGCAAGCAGCAGGAAGTCATGTATGAGTATGAACTG  
ATCTGTATGCAAGGGCGGGGAGAACACGCGGAGGAATGGGGCGTGAGAAA  
ACAGCACAGTACGTTTCTTAGCAGCTGTCTCTGCTCAGCCATGGGAGTC  
ACCAGAGAAAGAGGCTTGGAGGCGTTATTTTCACTGTGAGATGTGAGTGT  
AAAAAAGTGCCCAAGACACAGTGAGTACCAGGGAGATGCCCTCTTTCCCT  
ACCCGAATGCAGAATGGCCACAGGCCTTAAACACACACATGGTTCTCTCA  
GAGGAGAGAGGCCTCCACAGTGGACACCCGCATTCTCCCTGGTCAGCAG  
CAGCAGGGCGAGTGCTGGGCCATCATGAAGCTTACAGGCAATGAGCTCT  
CAGCAATAACAGGAACAGTGCCCTGGGGGACTGTAGCTGCAAGACCGATTT  
TCATGTAAAGATGGCCTCTGAGGACTCCGAGATACACCAGGCTGAGACTAG  
CTGGCAGCTCCAAGTTCTTGGTCAGAAGAGAACAGGAAC TAGGGAAATTG  
GAATTACTGTTACTACAATTCTTTTACATCCGCACAACCATGAGGTCCAG  
AGAGTCTCTCTTATTTTTTTTTTAAAGACAGGGTCTCACTCTGTGCCCCA  
GCCTAGAGTGCACTGGTGTGATCATGGTTCAGTACAGTCTTCACTCTCCA  
GGCTCAAGTGACCCTCTGCTCAGCCTCTCAAGTGGCTGGGACAGCAGT  
TGCATGCTACCAGGCCTGGCTTTTTTTTTTTTTTTTTTTTTTTTTTTT  
TCGGTAGAGACTGGGTCTCTGTATTGCCAGGCTAGTCTCGAACTCCT  
GGGCTCAAGTGATCCTCTGGCCTCAGCCTCCCAAAGTGTGGAATTACAG  
GCATGAGACACTGCACCCAGCCAGTATAGTCTTTTAAACAGCTTTATTGAG  
GTACGGCTAACATTGAAAAAACTACACAAATGTAAAGTATGCAATTTGAT  
AATTTTGACAAATGTACACACCAGTGAACTATCACTACAGTCAAAATAA  
TGAACATATCCATCACTCCCAATTTCTCAGCCCCCTTGGTAACCCCTCT  
CTCCCAACTCCCTGCCCCCTAACATCAGACACTACTGATGCATTCTGTC  
TCCATAGGCTCATTTACATTTTCTAGAATTTTACATAAATAAAATGACAG  
AGTATATACTCCTTCATGTATGGCTTCTTTCAGCCCAATTATGTCAAGAT  
TCATGCTTATGGCTGTGCGTATCCTTAGCCCATCTCTTTGTCTTGCTGAG  
TAGGATACCATTGCATAGACAGACCACAGCTTGCTCATCCATTCACTCTT  
GACAACGTTGAATTGTCTCTGTTTTTTGCAATGACAAATAAGGTTGCTAT  
GTACATTCTGTATAGACATTTGTAAAAGCACAGCATTTCACTTCTCTTG  
GGTAAAGACCTAAAAGTGGAAAGGCTGAGTCATATGGTAAATATATATGT  
CTAACTTTTTAAGAACTGTCAAACCTGTACCCAAAGGGATTGTACAATT  
TTACATCCCCACCAGCAGTGTATGAAAATCCCGTACTTCCACATCCTCA  
CCAAATATGGTGTGGTCAATCTTTTAAATTTGGACATGNTAATGAGTG  
CAAAATGAGGCCCAGAGTGTCTGAAGTTACATTTGTATCCTTTTTTGGCAT  
CCAAAACAGGTGTCAAGCATAGAAAAAACACTTGTTCCTTGAATGGTCAG  
TCATTTACAAGTGAATTCAATACAAACCGGTAGTTCTACTGGGTAAAC  
TATGCCTTACTGTCAACAGGCACATACACATACAGACAGACAGGAAGGCA

FIG. 3 (49 of 52)

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CAGAGACAAGGCAGAGC...TGATAAGAAGGTGACCTGGGCTCTAGCTC2  
GCCTATCACCTAGTAAAAATATTAGTTAAGTAGCCATGAGTAACTCACTTA  
ACTTACCACAGGCTCCATTTTCTTATCTGTAAAAATAGGAACATTGAAACA  
GCTAATCCCCAAGGTTTGTGGATAATCAGAATTACAAAGATCAATGACAT  
TTCTATGAGAGAAACATATTTCCAAGTATTTGATGGAGTACATCAGACAC  
AAAGGAAAGGAAACTGAATATTTTGGAGTTTTTTTTTTTACCAAGAAA  
TTACATTTTGTAAATTTTTCAGAACTACCTCCTGAGGAAAGTGTAGCTG  
CACCCATTTAGAATGATAGAAAACATCAATCTGTCTGATTCCAAAGCCAA  
GTTCTTGTCTACAACGAGAAATGAAACAACCTGGATCCCTACAGATGCAGAG  
ACCTGGGCCCCACAAATGTGAATTCTGTTCCCTACCGAATAGAGTTACA  
GTTCCATAATACAGTACTCCCTCACTTTTCCACAGTCTCACATTCCACAG  
TTTCAGTTACCCACAGTCAACTGCAATCCAAAAATATTAATGAAAAATTC  
CAAAAAATAAACATTCAGAAGTTTTAAATTTGTGCTCCATTCTGAGTAGCG  
TGATAAAATCTTGTGCCACCATCCCACCTGTCCAGCTTATCGTTAGTCAT  
TGACATCGTCTGCTCCTGACATCCAACCATTGACATCATCATGACTCTAT  
GATCCAGGATCACCGAAGCAGATGACCCTCCTTCTGACATATCATCAGGC  
CAATATCAGCCTAAACACTGCATCACTATGCCACATCAGTCACCTCACT  
TCATCTCATCAAGGAGGCAATGGATCACCTCACATCATCACAAGAAGAAG  
AGTGGGTATAGAACAATAAGATAATTTGGGGCAGGCATGGTGGCTCAGC  
CTTGTAATCCCAATACTTTGGGAGGCCAAGGCAGGAGGATCCCTTGGGCC  
CAGGCATTTCAAAACCAGCCTGGGAAACATAGTGAGACCTCCTCTCTCTGC  
AAAAAAAATAAACAAAAATATCCAGATACAGTGGTGCATGCCTGTGGTC  
CCAGCTACTCAGGAGGCTAAAGTGGGAGGATCACTTGGTCCCAGGAGGTC  
GAGGCAGCAGTAAGCTGTGATCGTGCCACTGCACTCCAGCCTGGGCAATA  
AAGTGAGACCTGTCTCAAAAAAAAAGGTAATTTTGAGAAAGAGACCAC  
ATTATACAACTTTATTATAGTATATTGTTAGAATTGTTCTATTTTCATT  
ACTTATTGTTGTTAATTTCTTTCTTGGCTAATTTTTTTTTTTTTTTTG  
AGTCGGAGTTTCACTCTTGTGGCCAGGCTGTAGTGCAATGAGACGATCT  
CAGCTCACCGCAATCCCGCCTCCCGGGTTCAAGTGATTCTCCTGCCTCA  
GCCTCCCGAGTAGCTGGGATTACAGGCGCCTGCCACCATGCCAGCTAAT  
TTTGATTTTTTAGTAGAGGCGGGGTTTCTCCATGTTGGTCAGGCTGGTCT  
CGAACTCCTGACCTCAGGTGAGGCCTCAGCCTCCTAAAGTGCTGGGATTA  
CAGGCTTGAGCCACTGCGCCTGGCCTCTTGCCTAATTTATAAATTAAC  
ATTGTCACAGGCATGTATTAATTTATAGGAAAATCATAGACATATAGAGT  
TGGGTACTATCCACAGTTTCAGGCATTCACTGAGGGGCTTGGAACACGCC  
CTCCTCAGATGAGGGGGGACTACTGTCATCTCCTCAATCATTCTTGATTC  
AATCCTCAACACAAATGGTTTGGCCAGGTCTTGCCTCTGGAGACAAATTT  
GCTAAGGATTTAGAGGGGAAAAAATGTAGTTCACTGGGAAAGTCACCTCT  
GCTCCACTGGACAGCAACTTAAACCCAGGCCATGACAAGTAGAAAGGCC  
ACCCCCACTCTCCTTACACCTGGAGTATTCAGGAGTCAATCATATTTCA  
GGACCACCAGGAGCAAACTGGGAAAACTGAGCTGCCTTGAGGAAAGCAA  
TCAGCTCCACAAGGGGCTTAAGAAACAAGCTCTGGGAGGAGTGGTTGGAG  
AAGAGTTGGGGACACATCAGAAATGCCATCAAATTTCTAAGGGCTACCTC  
GTGGTGTGAGACCTGTGCATCTTCAAGGACATAAACAGATGGGATAAGCA  
GATGAGATTACAGAGGACATCAAATATTGGCTCCCCAGAAGGGAGAAC  
ATTCTAGTAACAGAGCTGCCCAGCTGCAGAGTGGACTGTTTCACAAAGCA  
ACAGGTGCCCTGCCCTCTTGAATCACCATCTTACAGGAATGCAGTAGAAG  
GGACTTAACTCCTGCCCTGAAGAAAAGGTTAGGCTAGGGAACAGCTCCA  
AAATTTTTTAAAGGAAGCAACATAGGCATCTACTGGGAGTTTTCTAAAG  
CCTTTGTTAATGAACTAAAGAGCTGGGACAGGAAATGCCAAATTAAT  
TAATAGAGCCTTGCTTTAAGACAATGCAAGTGGATGGTAATGAAGGAATG  
AGTCTTAGGCCTTGGATCAACCGTATTAAGCAATGCTGAGCATGGAGCCA  
ATTCTGTTCACTAGATTTGCTCAGAAAGGGCCAGACGAGAAGGATTTTC  
TAAAGGCACCTACTACCAAAAAGCTGCCAAGGCGTCCAATGGAGCCGAGA  
GAGAATATGCTAACAAATAAAAAGTTGAACACCCTCAATAAAAAAGGGTAA  
AAGTAATTAATAGAAAATTACTGAAAGCTTTTTTGAACCAAAAGTAGTC  
AGCATTGGTAAAAGTCTACAAAAGTGGACACTTTCATATAATGTTGGCAG  
GAGGGTAAAAAGACATAACCTTTTGGAGGACAATTTGGCAACAGAGTAC  
CAAAAACCTTACAATTGAAGAGAACTTTGGCCTGAGTGCAGTGGCTCACA  
CCTGTAATGCCAACACTTTGGAAGGCCAAGGTGGGAGGATTGCTTGAGCC

FIG. 3 (50 of 52)

CAAAAGTTTGAGACCAGCTGGGGTAACACAGTAAGACCTCGTCTCTATG  
AAAAATAAGAAAAGTTAGCTGGGCATGGTGGCATGTGCCTGTGGTCCCAA  
CTACTTGAGAGACTGAGGCAGGAGGATCGCTTGAGCCTCGGAGGTCAAGG  
CTGCTGTGAGCCATGTTTCATGCGACTGTTCTCCAGTCTGGGTGACAGAAT  
GAGACCTGTCTCACCAGAAAAACAAGGCAAGAGAGAGAGAGAGAGAGAA  
GGAGAGAAAAGAAAAGAAAAGAAAAGAAAAGAAAAGATGGAAGGAAGGAAA  
GAGAAGAAAAGAAAAGAAAAGAAAAGAAAAGAAAAGAAAAGAAAAGAAA  
AAGAAAAGAAAAGAAAAGAAAAGAAAAGAAAAGAAAAGAAAAGAAAAGGA  
AGGAAGGAAAAGAAAAGAAAAGCAAGCAAGCAGGAAAAGGAAGGAAGGAAG  
GGAAGGAAGGAAGAAAAGAAAAGAAAAGAAAAGAAAAGAAAAGAAAAGAAA  
GAAAGAAAAGAAAAGAAAAGAAAAGAAAAGAAAAGGAGAGGAAAAGGAAA  
AGAAAAGGACAAAGAAAAGACCTTTGAACCCCTGAATTTCACTTTTAGAGA  
TTCATCTTAAGGAAATTCATTCCAATAGAAATTTATCCCCAGGATTATCT  
AAATATTTGCTTTTATTTTCTTCTAGTAATTTTATGGTTTAACTTTCTCA  
TGTTTAAGCCTTTAATTTATTTGGAATTTATTTTGGTATGAGAAAGTGTG  
ACCTTTTTTTTGTTTTACTTTAAAAAAAATGTATTACGATTATTTTATTTAG  
AGACAGGGTCTTGCTCTGTCAACCAGGCTAGAGTGCAGTGGTGTGATCAT  
AGCTCACTGCAGCCTTGAACCTCTGGCCTCAAGCAATCTCCCTCTTCAA  
CTTAGGAGTAGCTGGGACCACAGGCAATGACCACCATGCCCACTAATTT  
TTTTTATTTTGTAGAGACAGAGTCTTGCTTGTGTTGCCAGTCTTGCAAT  
GTTGTCTCAAACCTCTGGGCTCAAGTGATCCTGTGCCCCAGCCTCCCAA  
AGCACTGGGATTACAGTGTGAGCCACTGCGCCAGCTGCCTTTTATTT  
TTTAAATTTTTCAGATGCTTTGTTGGTTCCAAAATAGCACTTATTAACCCA  
CGCTTTCCCTCTGGTTTTAAATACTGCAAGTTTGGCTTTGAAATACAA  
CCCACTGCCTTATTCAGGCTACATTCAGGAAATCTGAGACCAAGAGTCT  
GAAGGCCAGTTTCTTCTCAAACCCAGGAGGTGGTAAATGTGTCACTT  
CCACACTTTCTATCTATTTCTAAGAACTCCTTCTTCCAACTCTGACAT  
GCCCCCTGGCTCAGGTCTATAGAAATCCCAGGGTCCACAGACAAAGCAGA  
ACTCACTTATGGGAAATCTGGGAAATCTTATCTGTTAAACCTGCCCCA  
TATGGTGACTCAGATTGTCTAAAGCCCAAAGCATCAATTTCCACCCCAA  
CCATTTCTCTCTCAGACTTCTCTATTTCTGTGGTCCAGAGTCAAGATCT  
TGATATTACCCTAGAGTCCCCCTTCTGCTCTCTGCATACCAGATGCCC  
CTCCCTCCCAGATCCATTCTCCACCTCCCTCCCATCAGTTTGGTGGG  
CCCATCACCGCTTCCCCTGGCCAGGCTCTCCTTTTGTGCGCTTGGAGCA  
GCAGACTGATCTCCAGCCTTCACTCACTTCATGTGGTAATCTGTTGTGT  
TCATCACTGTGAGAACTCTCTGCTATCCCTCACTACTCTGCTGAAAACAC  
TCTAGTGGTCTCTCATTGCTCATTAAATGAAAGTCTAGATATTAACGCTAG  
AAGGCCAGCACAAATTTGCCCTATGCCACCTACCTCTCTAATCTTTCT  
CCTTACTCTGACAGACTCTCCGTCTGTCAATTTATGTATTCTTTTATTGCT  
CTCTTCTACTTTTAGTATGAACTGGATTTATGGATTTTTTTAACATTGCT  
TTCAAGTATGGAATAAAGAATTTTATTTATTTATTTATTTATTTGA  
GACTGGGTCTCACTCTGTTGCCAGGCCAGAAATGCAATGGTGCAGTCATA  
TCTCACTGTAACCTCGAATTCCTAGGCTCAAGCCATCCTCCTGCCTCAGC  
CTCCTAAGTAGCTATGACTACGGGTGTGCATCACCACATCTGGCTAATGG  
AATAAAATATTACAATGCCTAATCTTAATTTTCAAATTTTAAATTACAT  
TGTACCTAATGCCCATGCATTTACTTTTTTCACTGGGTCAATAGCCCTCA  
CTTTGGCAAAGGTCCCAGGCCCAAGGTAAGGCCTTACTTTTTTCAAACCTC  
ATCTTTTGAAAGACATAAGTGCCTGTAAGTTGTACCACATTAGGTTCTAG  
GAATTTTTTCAACAAAGACTTTATCAGACTATTTTCTCTAAGTTGAGAAA  
GAGCTGGGGGCAGAATATGGCACTGAATGACTGAAGAGAAGGCACTGAAA  
TCAGGCCAGAGGTTGCTGGAAAGAGCAATGAGGAACACCAGCAGCAATGA  
GGAGCCGGTGATGATTTTGGCTTACAGGGAGGTGTGTACCACACCGATT  
TTATCTCTACGTGGATGAACCACAGCTGTGGCTCCCTTGTCTCCAGGAC  
ATCACACTCTCCACATTCCTCCCCTCTTCCGGCTTCTGCTTCCCGGGC  
CCTCATCTGCCCCATCCTGGGTGAACACTGGTCCGTCAACTGCTGGGCGT  
ACCTTCCCGCTCTGCACACCTCCCTGGCCACCCACCCACTCTCACGGC  
TCGCACTGCAGAGGAGCCGATCTCTAGCTCCAGCCCATCTGCCTCTTCT  
GAGCTCTAACTTCAAGCAATTTTCCCTCAGAACCATGTCTGGCTGCTCC  
ATCATACTTCAAAGCAATTTTCCCTCAGAACCATGTCTGGCTGCTCC  
CTCCAGAAGATACATCTCTCAAGCACATCCCCGGGCTCTCACCTGGATG

FIG. 3 (51 of 52)

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ACTGCATTACCTTCTC ACATTTGCCCTCCTTTGGATGTATATAGA.  
GTTTTAAATACAAATCTGATGTGCTTGCTCTCCTGCTTGAAACACCTCA  
AAACTGCCTTCAGGATAAACCACTGCCCTTGACATGTTACAGGTTGCCC  
ATGGCCTGGCCCTGCCATCTCTTCAGCCTCATCTCATGCCCTTGCCCC  
TCGCTCTCTGGGCTTCTGCCTCCCTAGCCCTCCTTTAGGTTCTCTAACAC  
ACCATAGTCTTCTAGTGTGGGGCCTCTGCAAGTGCTGTTCCATTGCC  
TGAGACATGAATCCCTCTCCCTATCTCTACCTGCACCTTCATCTGATTAA  
TCCCTACCCTTCCTACTCATGATGTTGCTTTCTCAGGGACTCTCTCTGAC  
TTTTTAAACTAATCAGGGTCTCCCCAGTATATATCTTCATAGCACTCTGT  
ATTACTCCTTTCTTAATGACCACCTGCTGTAGACTGAATGTTTGTCTTCC  
TCCAAAATTCATATGTTAAACCTAGCCCCAAATGTGATAATATTTGGAG  
GAAGGCTCTTTGGGAGGCAGAGCCCTCATGAATGGGATTAGTAGCCTTAT  
AAAAGAGACCCCTGAGGGCTCCCTTGTCCTCCCTCCACCGTGTAAGGATGCA  
ACAAGAAAGTATGGTCTATGATCCAAAAGCAGACCCTTGCCAGGTACCC  
AATATGCTGGCACTTGAACCTCCAGCCTCCAGAACTGTGAGAAATAAAT  
TTCTATTTTTTCATAAGCCACCGAGTCTATGGTATTTTGTATAGGAGCAC  
AAACAGACTGATGTGCCACCCCAACCATGATTATACGTGTAATTTATGGTT  
TCTCTGCTAGTAGGGATGCACCATGGGGTTAGGAACACGCTTTTCTTAT  
TTCCACACAGTCTTTAGCTCTAAGCATGTTCTGTAATCAAAGATCCCCA  
TCTTTTATGAATGAAGGAGTCAGTGAATGAATTAATGAAAGAACTGATAA  
CCCTCAATAATTATTCAGCCTTTTATACCTACTATTAACAAGCTTGCAAT  
TCTACTCCAAATTTATTTGGGCTTTAACTCTATTTTTTGGCCAGCCACATTT  
GACATTCCTCTGAAGTAAATCTATGCTTTCCATCCTAAGTCAAGGAAGGAC  
CTGGACTAGTAGGGCCAGAAAGGTCTAAATTCATGGGTGGGAGAGAGA  
GACTAAATCTGAAAGGAAGAATAGATTGAGCAAAGGTGTAGAGATTGGGG  
AAGGCTGGACATTTGGAGAGAAGGAAAAGGAAACTGACACTAAACCAAAC  
AGTCTCACAAACACAATCTCATCTCTTCCAAAACCTCTGTGAAGTAAGAATT  
ACTATCCCAGGGCCAGGCACAGTGGCCCATGCCTGTAATCCCAGCACTTT  
GGGAGGCCAAGGTGGGTGGATCACCTGAAGTCAGGAGTTCAAGACCAACC  
TGATCAACATGGTGAAACCCCATCTCTACTAAAAATACAAAATAGCTGG  
GCATGGTGGTGACACCTGTAATCCCAGCTACTTGGGAGGCTGAGGCAGG  
AGAATCATTTGAACCTGGGAGGTGGAGGTGTCAGTGAGCAGAGATCGTGC  
CACTGCACTCCAGCCTGGGTGACAGGGAGACTCCGTCTCAAAAAAAAAAA  
AACAAAAAAAAAAACCAAAAAAAAAAAACAAAAACAAAGAACTTACTATCCCAG  
TTTTGCAGATGAGGCAATGGAAGCTCTAAAAAGTTAAGTAGGAGAAACAA  
ACATGAAATGTATGTCTTATGCTTTTCTCATCCTATTTCTCAGCCTGG  
AATGTCCATTCTCCCTCCACTATGCAAATCTAACTCTTCAAGCTAACACA  
TAGCAATGTCTGAGAAACCGTCCCTGTGTTCACTCTGTTAGCCTCACTTG  
CTCCCTCCCATCCCTCTGTTTCTTTCTGTTATAACACTTCTCTATTCT  
GCTGGCATCACAGTCATCTCCACCTGCCTTCTCACAAGTTAAAAGCTTG  
TTAAGGGCAAGTGGTGTCTTTGCCACCTCATTCCCCAGGGCTTCTAACA  
CAGTGCCTCATGCATGACAGAGTTGTAAAACAGGTTACCAAGCTGGCTTC  
AGGCAGGTTTGCATGGAAGTGTGCTTTACAGGAATACCTGCTCCCCCAG  
GCCCTGGGTCTTCTCCTGAGTCCAGGCTCAGACTCTCTCATCCTGCTCG  
TTCTCTCTTGGGGAGCCACAGTAACTTTGAGCAACTTTGCATGGGATAGA  
ATGGCCTATTAGGGGCAGCACAAAGACCCCATGGAGGGAAGAGTACAGAA  
AGGGAAAACGATAATCATATTTTTTTAAGATGTGCATTTTCTTAACAAAA  
TGCTCTAGTACTTGTCCAGACTTTCAAACCTCAAAAACCTAAGCGTCTTTT  
TCTTGAAGATCATCAAAGGCCCCAGTGGTCTTCAGGTATGTCAAGCTTT  
CTAGAAAATAAAGGTAAGTCATAATCACTTAACACACATGGCTAAATGGC  
CATTTCTTCTAATTTATCAGCAACTGTTACATATTTCTATACTAGAAAA  
AATTTATATTTATACTCAGGGTGGTAAGTTAAATTTGCCATCGAAGTAAA  
GCAGAAAGAGCGTAGCATGTATGTATATGTAACCTCACTGTGCATGAGAC  
AAAGATGTCTTGAGGAGAATGAGTCTAAGATGCGCCTGAGCAATAGTACC  
C

FIG. 3 (52 of 52)

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>Contig1  
GCACCCATGTTTCTAAAGGGCATACCAGCCATAATAACAGGATGGGTGAG  
GATATAGACAGCAGATGACAGAGAGAGAGTGAAAGCTGGGAATCCCAGC  
TAAAGGCATCAGGTTTATGGAATGAGTAGGGGACAATACTGTGTGTGTTT  
ATACACACATGTATATGTGTGTATATGTATACATGTTTATGTATATATAT  
AATTATATGGTACCATTTCTAATTGACAAAATAATCTATCACATTTTACA  
TTATCAGATTTTACATCTATTGTTCTAAATACACTCAGTCATCAGCCCTG  
TGTGTGGGCTCTTACCCATCCCCATGCACACCTCAGCTCAACCACTGATG  
GATGGATCATCTGCCTATCAGAGGTGGCATATTCAGGTGAATCCATGGCC  
ACAGCTGCAGCACTTCCTACCCACGCAGAAAGGCTCCACAAGAGGAGGCA  
CACCCGCTCTGACTGTCCCTAAGCTCCTGACATCTTACCCCATGAACT  
GCTGCTCCTGGGTGCTTCTGCTTGCCTTGCCTGCCACCCTTGACTGTTCT  
CACCATTGACACAGCTGGTGCCCGATGCAC

>Contig2  
NAAAACGAATCGTCACTATTGAAGCCTGTCTCTCANC GGATCGTGACTAA  
GAACCCCTCCTTGCTTCAAGTTGTCTGCTTCTTAGGCAGAGCCACCC  
TACATCTTAAATATATTGATTGATGACTTACGTCTCCCTAAAATATATAA  
AACCAAGCTGTGCTCTTACCAACTTGGGCACATGTGGTCAAGACCTCCTG  
ATGCTCTTGTTCATGAGTGGGTGGGTGTTCTCAACCTTGGAAAAATAA  
TTCTAAATTAACAGAGCTGGGTGAGATTTTGGGGTTCACAGCAACAA  
TTTAAAAAATCACCATTGACCTGAAATTTTGACCTTATGCTGTTGCTCA  
CACTCCTCCATGAAAAATAGACGCCATCCTATGAGTTCCCTCAGCCATGTC  
ATGCCACACTTCCAACATGTGTCCCATCCACCATCTGTCTTCTTATTGC  
TGCATCCTACCCAGGCCCTGATCTCTGGACCCATGTTGTATAATTAAGA  
ATTTGGGGCTGGGCATCGTGGCTGTGGCTCAGCTCTGTGATCTCAACATT  
TTGGGAAGGTGTATTAGTCAGGATTCTCCTCCGAAGGATGCAACCCTAGGGA  
TCCTCTCTATGACCCTATGTCTA

>Contig3  
CGCGCTCAACCGACCGATTTGCGCGAACCTGCCCCATGCCCCGAGGACAGTG  
TAATCCTAAAACGTCCCCTGAATCATAAGGATATGAGTGCGAAAGTACGG  
TTCCCTCTGTCAACACTTTCTAACAACGCTATGTCCGATCCGTGCACTAA  
CCCCGCCCAAGTCACTGAAACACTGATGGGCGCTTCTCTACAGGTATCC  
AGGGCCAATACCACTACTCCCTCCTCCCTGTCCCCCTTCCACTCTCTAG  
AGGCGCGGATGCGATCCTCTATTAGCACAACCGAAAACGACGGTGAAAG  
TACCACGAAGCTCAGCATCTGATCGGTGCGCCCAATGCGGTACAAACGGCT  
GTCATCCCAACCCCGTCCCATCCTCCATATTGCCCCCCCCCTATGAGGAT  
GGCCCTATCATCATGACCTCCAAAATTCTGTCTCTCCCGACGTAATGCC  
GCCCTCGAACGCTGACACCATCAAGTCNGTCACCTCCCAAAATACTCC  
TCCTAATCACCAGGCCGAGTATCCCCGTTCCACAATACTCCTTGAGAC  
GGGCCGATATCACACAC

>Contig4  
NNGAGTTTAGGTCAACTAGTAACAAGTGGGATTTGCGACTCAGGTCTATC  
TAATCCTCAAACCCACGTCTGGACCCCTACACAGACTGCCCTCCCTCAG  
TCCTCTGTGTGGCCTCAAGAAGGGTCTGGACATTCAAGTTTAAAAATCCA  
TCCAAAGAATCTATGGACCCAGTGGTCTCTGGAGTCAATGTTCTGAGGCT  
CAGAAGGGCCAGGCAGGAGGGAGCCGCTCTACACAGTCTGAGCAGAGT  
GGGCTGTGTCCCGGCACAGCAGGGGAGATCATAAACAGAATTCTGCCCTG  
GGCCCTATTTAAGTAGGACCTTTAGGCTGCCGGTGTGATGACCACAGGTC  
CCANGTCTGCACGATTGGCTGTGTGTGGAAAATCTTCACTCCTTGCGGCC  
TTGTCTTGGCAGAGAGCACCGCTGCTTCTCTGATGGCCACCAGGGGGA  
GGCGCTCCCTGGGAACGGTTTGAANGGGAGCCTCACCCACACGTGCCT  
TCCGTGGTACCCAGCACAGCTGCTACCCATGGTTACCCACAGGCCACG  
TCTGCTCTGAAGAAGGAGGAGTGGTGGCGATCANGCCTTGTCTGCATCCC  
GTGGCTGCCCTTTCTTTCTTT

>Contig5  
GGGAGCTAACCGCTCACTGGGATTACAGGTACGCACCACCACGCCTGGCT  
AATTTGTATTTTATGAGAGACGGGTTTCTCCGTGTTGGTAAGGCTGG  
TCTCGAACTCCCAACCTCAGTTGATCTGCCCGCTCAGCCTCCCAAAGTG  
CTGGGATAACAGGTGTGAGCTACCATGCCTGGGCTTATATGTTTCTAGTC  
CAACATTTAGCTACCTTTTTTTTTTTTTTGGAGACGAAGTCTCACTCTGT

FIG. 4 (1 of 61)

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TGCCCCAAGCTGGAGCACAGTGGGCACAATCGTGGCTCGCTGCAGCCTCAAC  
CTCCTCAGGCTCAGGTGATTCTCCACCTCGGCCTCCCTAGTAGCTGGGA  
CTACAGGTACGCCACCTACACCCTGCTAATTTTTTTGTTTTGTATTTT  
TTGTACAGATGGGGTTTTCTCATGTTACCCANGCTGGTCTTGAACCTCTG  
GGCTCAAGCAATCTGCCTACTTCAGCCTCCCAAAGTGCTAGGATTACAAG  
CATAAGCCACCATAACCCGGCCTACCTACTTTTAACTTGTGGAATTTTCTA  
TAAGGTCANGGATGCCTGNGGGAACAAAAGTTTCTCCCTTGGTATATGCA  
AGTAAAATCCACATGCTGCCTCCC

>Contig6

AGGACTGTAGCTGTTGTCTAGTCACCAGGCTGGACTGCTTGGCATGATCT  
CAGCTCACTACAACCTCCACCTCCTGGGTTCAAGGGATTCTCCTGCTTCA  
GCCTTCCAAGTAGCTGGGATTACAGGCATGCACTACCATGCCCGGCTAAT  
TTTGTATTCTTAGTAGAGACGGGGTTTTCGCCATGTTGGCCAGGCTGCTCT  
CAAACCTCCTGCCCTCAAGTGATCTGCCTGCCTCGGCCTCCCAAAGTGCTG  
GGATTACAGGCGTGAGCCCCCGGCCACATGTAAAAGTTTATATCTCTGT  
TGTTTTACCTTGTTTTTGACCTAGTCTTTCAGTGATTTGAATCTTGATTC  
AGTCTTTTGTATTTTAGTGGTACTTCCAGCTTTGTGTCTATCTGTGGAT  
GACATATAGTCTTGCTTCTTCATGCCAATTTAAGAAGACTGAACGGGAA  
TAGGTCAAAGGCATGGCCATGAGCGATTTCTCTCCAGCTTTTCATGGTGT  
TCAGCTTCAAATCTATTACATATTGGACCTGCAAGCCATCATCTTATCC  
ACAGGCTATCATATAGGTGAATGTAAATTGGGTTTAGGTGGCCAAGCTG  
AACGTGAGATATNTTC

>Contig7

AGCATGTTCTCTAAAGGCCTATCAAAGCTGACATCAAAGGGATAAGTTCC  
AGTTACCCAGCTGAAGGGAAGGAGGTGTTTCAGATAGAGGAAGGATAAG  
CATGACCTATTCAAGGCCAGTGAAGAAGCGTGCAACGGCCAAGTCAGGA  
GAACCTGAAATTGTGTCAAAGAGCTTGGATGCAAAGAGCCGTGGGAGACT  
ATTGGGGGTTTTAAGCAGGGATATAATATTCAATCAAGCATGCAGTAAAA  
GGTCACTGGCACCTGCCATGGGCCAGGACTCGGGCTCTACATGATTGCGT  
CTGTTTTTGAAATATCACCCCTGGCTGTGAGATGAAGAACAGGTAGGAGGG  
TCACAAAACCTGAAGCAGAGAGACTGTTGAGGAAGTAAGCTGTTTTGTG  
TGGACTGTGGCAATCACAGAGGCAGAGGATATAAATGCACAGAGACACAA  
GGCATGTGGGAGGCAGAAGGAATCAAATACAATGAGTGATCAGATGTGGG  
GTTAGAATGGTGAGTGANAAAGACATACTCAAGGTGACACGCCAGGTAT  
CTGGGTGGATGGTAAGACATTATGGAAGTAGAATCGAAGAGGAGGTGGG  
ATGGACATTCTTCCGTTTAGAGGGGTTACCAGGAGGATTGCGCGAAC  
ATGGAGAGGATTAACCAGGAATCCGGTGCTTTTTTCAAACCTGGGTGGA  
GGGG

>Contig8

GGTGAATGCTTTGGCACGCTGTGTAGATTTTAGGTGACGGGTGGTGACAA  
TGAGTCCGTGTGAGCGCTGATTTTTTCGGCCTTAGAGCGAGATTTATA  
CAATAGAATTTGGCATGAGATTGGATTGCTTTTAGTCAGCCTCTTATAGC  
CTAAAGTCTTTGAGTGACTAGATGACATATCATGTAAGTTGCTGATAGGT  
TTCCAGTTTTCCGCTCCTAGGTCTGCATATTGTACTTTTCTCTTACTCG  
ACTTAACCACTACCAACCCAGCTTCTCAACGGATTTATACCATGGCACTT  
TAAAGCCAGCATCACTGACAATGAGCGGTGTGGTGTACTCGGTAGAATG  
CTCGCAAGGTCCGGCTAAAATTGGTCATGAGCTTTCTTTGAACATTGCTCT  
GAAAACGGGAACGCTTTCTATAAAGAGTAACAGAACGACCGTGTAGTGC  
GAATGAAGCTCGCCATACCATAAGTCGTTTTTGTCTCCCGAATATCAGACC  
AGTCAACAAGTGTCAATGGGCTCGTATTGCCCGAACAGATTAAGCTAGCA  
TGCCAACGGGATAAACGAGTCGCTCTTGGTGGAGGG

>Contig9

GGGGTGGGGCGCCTGGTGTCTTCTAAAGAGGATCTCCTGCCAGAAATGGTG  
TGCTGACACTGTTGTCTCTCTTGGTGTGGAACCTTGGTGGGAAGAAAGGT  
TGGAAAGGGAATTTGATCCTTGGATTAAACCCGAGTTGTTACTGATG  
CTCACAAGACTATGGGAAGGATAAAGGCAGGTGAGTCACTCTAGGATGGC  
TCANTGAGCTCCACAGAGCTGGAACCAAGGCACCAGGAGGGATTGAGAG  
CAGGCCTCAGTGCACGTGAGTGAACCAATGAGCAGGTGATGGGTC  
CAGGCAGAGCCCTGTCTCTTTAGGCAAAAACCTTGAAACACCGTTCCC  
ATCCTAGCCTGTGTTCCACCCAAAGCTGGCCAGTCTCAGGCCCTGCCTG

FIG. 4 (2 of 61)

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AGCCCCAAGGAAGTGGTATGGTGAAACAGAAGGGCCATTCTGTCCAATG  
TGTGAGGAACCTTCATTTAGACTTGTGGGAAGCCCTGATGTTCAAAAACC  
TCAATGATATCATTTCATTTTCCCCATCCATTCAATGCCCATCCAATGCCC  
ATCCGTTCAATGCCCCCTTCCATTCTCTTCAGGGAAATGAAAATTGTTCA  
GAAATCCTTTCTCTTTGAGAAACCAACCAAAACCAAAACCGCGAAATTCA  
CTAAACTAGCCAAGACACAATCCTGGGTTATTTTCTTTTCCCAAACCTC  
CTGTGTTTAAATTAATTCTACCCTGGTTCTCGGCCCTTACTGCGAAGGTG  
AACTCACCTAACCTCTCCCAAACAGAGAAGAACTTCTCTTGGTAAATG  
GGTTTTAACACTTCTAAAAAACCCCC

>Contig10

GCTATGGTTCTAAAGGTAATGGACTATGGCGTACACAACGTCTCGCTCAT  
CGTCTGCCAGGAGGCTAAGGTATCCACGGACAATCGCTGAGCAACAGTGT  
CGTTGATCCATCTCTGTACGCACTTGTCAACATGGCAGGAGTACGGGAGC  
TGCGAGAATCCTCTCTGTGATGTCCACGGAGCATGCCGTGAGACAACG  
CCACGAACGGCCCTCGGAGANANCTACTCTGCAATGAAGACGTACGATAC  
ACACGTAGGAGTCTTAGCTCACCAGCCGTATCTAGGTATACTGTACTCGC  
GGATACTCACTCGTGCATGCGGCAATAGATCGATACGCAGTCTGTCACGCC  
CATGCTCTCAGTGTGTGACCTTCTGGCGGTAGCGTNGTGGGCGCTATTAC  
TGTGCGCAGCAGGCGCTCGTACATGTGTGCGGTAGCGATGCCAGGAGCT  
GTAACATAGCAAGTCGCCCCCTACTCCTATCACTATCCCTACGCTGGAC  
CGCACTCGAGATCTGAACGCACGTCTTAACCTGCCAGTACTCGTGAGACC  
TACTCTGCGCAAGCCTTGGCTAGGAGATCCTGCAGCGCCGGCAAAGAATC  
AGCTATGATCCCCTTGGCATTATCGCACACGCACCATAGAGTATGTGCAT  
ATTAACCTCTGAATGTGCTGCAAGCAGACGGTTGCTCAACATATATATGG  
ATGTGGGGAAATCGCCCTGGTCACCGCACTTGGCGTCAGGAGGCACCAG  
CACGTCTGAGTGTACGCACGTTACTC

>Contig11

GGCCGAATGGTGAATTCATCCGTCTCTCGAGGGGGTGAAAGACGGGGAG  
TTATGCTGTAATGGCACCCTCACCCTGGGCTTATGAGCAGACCTAACC  
TCCCANAGTGCTGGGATTACAGGCATGAGCCACCCTGCCCGGCCAGTAT  
CTGAACCTCTGTGGCCAGGCAGAAAAGGTCCTGTGTTACTCGTCTCCTTT  
ATCATTATGTTCCATATTTCTCCATTTGCTAACATTTATGTTTCTGCTCC  
ACTGGATTCTTTGGATTTTCTAGAACATACCCATGCTTTGCATTGCCTT  
GGTCTTTGAATATTTGGTCCACTTTTCTGCAAAGTCCCCTCTCACCTTA  
TCTTCTGGTAAACTTCCAGCCAACACCTTTTACTAACCAGAGAAACAT  
GGTTCAACTGTGCACAGGCTTGCACAGAACTGTTCTCATATTGTCTTGT  
CATTGTCAATGTGGCAGAGATGCACCTTAGATACCTCTTTGAGAAAGGAC  
TCACTGCCCAGCTGCCCTGGCACGTGATGAGCTGATAGCTCCAGCTATAGA  
CTCCTTTAGGGTCAACCTCTGCTTTCCAGTTGAGATCATATCCTTTGCAG  
GGTGGCCTTCCCGAGTGATGACTAAGGCAGTGTTACAATGGCCTAGTCATT  
TCCTCCCAATGCTGGACTCCCAATGAACCATCTGCTCCGGAGCTTCCAC  
TGGGCAGTCAGAGACCTTAGCTAGTCTGCCTCCGAATCAGAAGGCTCTCT  
CTTGCCACTCTGGCC

>Contig12

GCTGTGTCTAAAGATTACGGCTGTAGTTCCAACCTCCCGCCGCCCTCTAC  
TGTGTCTCTTAATGGCAGTCATTACCATCTTCTGTCCCTCCCCTTCA  
TTTCTTGATGGTGAATGTCACCTTTGCTGCAACAGAACCCTGTCCCAATC  
CTTGATGGTTCAATACACATAGACATTCTTTTAAACAGGGCGGCCTCT  
CAGGTCTTTAATTTTCTTCCCTCCAATAACCTTGTGATGATCCCCAGCT  
TAGCCACTTACTGCCAGATCATTACCAGTAACCTCCAGCCCCTCCTTAATT  
CTAGTTTCTAATATCCTAATCTGTGACCTCACATTCCAACCTTCTTCATT  
TTATCCCCTGAGTCAAAAAATCCTTTGATCCATGCAATCCATTAAAGTCAT  
CTACCTTTTACCATTCTTCGCCCCACTAGGGTTCTCATTCTTTATTAC  
CCATATGAAATTCCAAGGCCTGTTGGAATCACTCCCTTGCAGCCACTGTC  
AATACTCTGCCCCCTTTACTTCATCACCCCTTATGTGGCAAAACCACAGC  
CCTGGTGGAGTCGATCCTTACCCCTGCTCTGTGCCAACAGCCGCACACGC  
ATGGCTGATGGAGGTTGGAAAAATCCACACATGCAAGTGGGCGCTGTATGT  
CCATATACGTATCCAACCTCCAGCCTTGCATATGCCTCAGTGTCTGCTGA  
CAACACATTATATGTTTTCTTAGTTCTTCTCAGTCTCCTGGGTGCCTAGG  
TGAGTATCTCAGACATCCTTCTCTCTGCAAAGCTCCAACACCTCCACG

FIG. 4 (3 of 61)

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TCACATTCAACTGATGACGTGTGTCTCCTATGTCACTTAGATCACAGAGGC  
ATACATAAACAAATCCCAGCCACTGCCAGCACTCTGCACATCTGCGAGCA  
TGGCACCCCCAATCTAGGCCTTTCTGCTGTCACTTGGGGTGAGCTGATT  
ATACTCGATCCTAGTCATTTCTACTTATGCAC

>Contig13

CTTAAGGCCTCCCTCTAACATTTTAATTTAAGATTGAAAAAGCAAAGATT  
ATTCTGTTTTGGCTGCGCCTATAGTAAAGTAACCCCTATGNCAAATTTTG  
ACACCTTATAGTATTTGACAGGGATAAGTATAAAATTGCTTGATTGATAC  
ATCCACACCCAAATGTATGCTGGGAATGATTTTGTTCACGGCACTCATT  
ACTTAATTTTTAAACTCTTATTTAAATTTGCAATGTTTTAAATGACCAT  
CACTTAAAGTAGTAATCAACAGAGGTTAGGAGAACATAACAATACTCTTT  
CTCTTAGAAAATACAACAGAAATATAATTTTTTACAGTTTGTCTCCCAA  
CTTTTCTCTGTAATAACATGCCTTACTCACCTTTACAATAGGTTTGTGT  
GAGAATCTTGTAATGTAAACCTGGGTGTTCTGTGAAGCATTTTTAAACT  
TCTAGTTTACACTGACTCTTATTCAAGTGTTTTTAAAAATATATTTAAAA  
AACTGGCCAGGTGCGAGTGGCTCACACCTGTAATCCAGCACTTTGGGAGG  
CCAAGGCGGGCAGATCACAAGGTCAGGAGTTTGAGACCAGCCTAGCCAAC  
ATAGTAAAACCTCGTCTCTACTAAAAATACAAAAATTAGCTGGGCGTGGT  
GGCGGGCGCCTGTAGTCCCAGCTACTCAGGAGGCTGAGGCAGAAGAATCG  
CTTGAACCCGGAGGCAGAGGTTGTGGTGAACCAAGTTTGCGCCAATGCA  
CTGCCAGCCTCTGCAGNGACAGCC

>Contig14

GGGGGCGGGCCGAGTGATCCTAAAGCCCGCTCGCTTCACAACAAAGCCTA  
ACAGTCCAATCACTTAATGCTGCATTTATTCCTGGGGAAGCAAGTCTCCT  
TTGCACTTTACACAGTGAGATAATCAGTTTCTCATGTGGACCACTGGGCC  
AGGAGGGCCTGACAAAGGGCAGTCTACATTTCACTGGAACTGCTCCC  
AGAACTATTTCTTTCTAGTTCCACCTCGGTCTGAGGTGCTGAGGAGAG  
GGACTCAACAGAGGAAGCAGGAGCATAGCTCAAAGTCTCAGAACATGGAA  
GAGGAAAAGAACTCTCACAAGATTACGTAACCTTACAGGCGTGTGCTGCT  
TCAGTAGAAGTTTCATCTCCCTCAATCCTGTACACTTTCCATACATTAC  
ATACTCAAACCTGGTCAGCCCTATGGAGCAATAGCAGCAAAAGTTATTCTTA  
ACAGTAATTAAACAATATAAAAGATCCCATTTAAAAATGGTTACTGGTCAG  
CCGGGCGTGGTNNNTCNANCCTNTAACCCCANCACTTTGGAAAGCATGCG  
GGCGATCCCAAGTCTGATATCGAAACATCTGCCTAACATGTGCAACCCCT  
CTCTACAAAATACAAAAATATCCGGGCTGTGTGTGGCGCCGTATCTCA  
CTACCCGGAGCTAAGTAAGAAATGCTTTACCTGGAAGCGATTTTCTTACT  
TATATCCCTCTCTTACCCGGGCGCGACCAAAATCTTTAGTATAGGAAAG  
TTTATTGTTTTATGCCTTTGTCAAGGCTCTACTGTATCTTTTCTGTCCAC  
TCAC

>Contig15

GGTTCTGAACAACAGCAGGCGATTCTAGCCCTGTACCCGGGGCATTGTC  
CAACACTCGACAGGGCTGAATTCGTCCATAACGGTGTGCCCTCTGGGAT  
ATAGGATGAAATGAATTGATCTGAGTACCTGGGATGTAAAGTTACTAAAA  
CGCCAGCTAGGTTACGCCCCGATGCTTAAATATGATCGTGGCCTACACC  
TCGTCCAGCAGAAAAAGTACCCTTTCTTCAACACCACCTCACGATCCTCC  
AATTTAGGAGCTATAAACTCATGACTCTTTATTTACCCCTGCAGATTCT  
TCAATCCAATAGTGTGTGTCTCCCTGTGAACTCACGGATATACCGATTTT  
CCCCACGTCAATTTCCACACGTGCAATCGCTTAGTCATCCCTATGTATGA  
GAATCATGGATGACTATGTTGAAGTCCATCTATAAAGTTCAACCCCATC  
TCCGTCCCTGATTCCCCCTCCCCAAGATCACCACGCGACTCGACATATT  
GTTATCGCCCAAGGGACCTCTTGCATCCCCCATATCCACTGGTCACCTCC  
CCTCTTGGCTGGAAGTACCCGGGAAGTTCTCCACATGTTGT

>Contig16

TGCGAGCGATGTTCTTAACTTTAGCGCCATTGACTCGAGCATGGTCATG  
GCTGTTTCCTG

>Contig17

AGGGTGTTCTTAAAGGATACTACGTTCCCTAAAGTCCAGAGAAAAAAA  
AAAGTAACATAATGTGGCTTATTTGGTATAAAAAATTTACAGGAAGCATT  
GTCAAATATGAAATAGTGTGTTGGTTTTGTTGGGCTGATTTGTATAAAT  
ATGTTATTGGTATGTGTTCCAAAATTATAGGAACTCCTATAATTCTGAT

FIG. 4 (4 of 61)

58/118

ATGACTTGGTGTACATTATCAGTAATAATTATAATTGTTATGGTAAATTA  
TTGTGTGCCATGGAGGTAACAAATTTCTCATCAAGTGTGCTTTGACTA  
TGGTTGCCCTAAAACCTTTTGGCATTACAGACAATTGTCTTGCTTTGGT  
CCTCTTTAGAAGGTGGTTTTATAATCAGCTATAAACTCTAACGGGTGCT  
CTTGAATGCAGGCTTAAGATAGCTTTGGAGACTGTGACATCAGAATAGAG  
GAAAAACTTTCAGTATTCATGGAGTGTGAAATATTCATGAATATCAAGC  
AAAACAGGAATTAACCTTCATAGATGGAATAAAAGAATGCTGAAGTAATC  
TTTTTGACTTTTTTCTTAAATGTTGATCCTTCGTTTTGTTTTTCAGAG  
TCAAGGAAATTTTTCTGTTGAGATATTGACAGCTTTTAAACAATTAAGTAT  
ACTCCAGTGAACACAATTTGGAGCATATTTGTGTCTCTCTATATATATT  
GGAAACAATNTTTGAGTATTCCTTAACCTTATTGCAATATT

>Contig18

GGTTGTCTGCTATACCAGTAATGGGATTGCTGGGTCAAATGGTATTTCTG  
GTTCCAGATCCTTGAGGAATTGCCACACTGTCTTCCACAATGGTTGAACT  
AACTGACACTCCCACCAACAGTGTAAAGCATTCTATTTCTCCACATCC  
TCTCCAGCATCTGTTGTTTCTGACTTTTTAATAATCGCCATTCTAACTG  
GCATGAGATGGTATCTCATTGTGGTTTCAATTTGCATTTCTCTAATGACC  
AGTGATGATGAGCTTTTTTTCATGTTTGTGGCCACATAAATGTCTTCTT  
CTGAGATGTGTCTGTTTCATATCTTTGCCACTTTTGTATGGGTTTTTTT  
TTCTTGCAAATTTGTTTAAATTCCTTGTAGATTCTGGATATTAGCCCTTT  
GTCAGATGGATAGATTGAAAAATTTTCTCCTATTCTGTAGGTTGCCTGT  
TCACTCTGACAATAGTTTCTTTGCTGTGCAGAAGCTTTTCAGTTTAATT  
AGATCCCATTTGTCAATTGGCTTTTGTGCAATTGCTTTTGGTGTCTAA  
TCATGAAGTCTTTGCTCATGCCTATGTCCTGAATGGTATTGCCTAGGTTT  
TCTTCTATGGTTTTTATGGTTTTAGGTCTTATGTTTAAATCCTTCTTTT  
TTTTTTTTTTTTTTTTGAGATGGAGTCTTAGTCTGTTGCCAGGCTGGA  
GAGCGAGTGGCGTGTCTNTAGGACGC

>Contig19

GCATGTTGTCTAAAGGTTTGTCTTCTCCAAAATTCATATGTTAAACCT  
AGCCCCAAATGTGATAATTTGGAGGAAGGCTCTTTGGGAGGCAGAGCC  
CTCATGAATGGGATTAGTAGCCTTATAAAAAGAGACCCCTGAGGGCTCCCT  
TGTCCCTCCACCGTGTAAAGGATGCAACAAGAAAGTATGGTCTATGATCC  
AAAAGCAGACCCTTGCCAGGTACCCAATATGCTGGCACTTGAACCTCCC  
AGCCTCCAGAACTGTGAGAAATAAATTTCTATTTTTTATAAGCCACCGAG  
TCTATGGTATTTTGTATAGGAGCACAACAGACTGATGTGCCACCCAAC  
CATGATTATACGTGTAATTTATGGTTTCTCTGCTAGTAGGGATGCACCAT  
GGGGTTAGGAACCAAGCTTTTCTTATTTCCACACAGTCTTAGCTCTAA  
GCATGTTCTGTAATCAAAGATCCCCATCTTTTATGAATGAAGGAGTCAGT  
GAATGAATTAATGAAAGAACTGATAACCCCTCAATAATTATCCAGCCTTT  
TATACCTACTATTAA

>Contig20

ACGGTTCTCTAAAGACTTTCAAGAGCTGGATTTTATGCTTTAGGTGAAGG  
TGATAAAGTAAAGTGCTTTCACTGTGGAGGGGGCTAACTGATTGGAAGC  
CCAGCGAAGACCCTTGGGAACAACATGATAAATGGCATCCAGGGGTGTA  
TATCTGTTAGAACAGAAGACACGAAAATATATAAACAATATTCATTTATC  
CCATTCACTTGAGGAGTGTCTGGTAAGAACTGCTGAAAAAACGCCATCAC  
TAACTAGAAAAATTGATACCATCTTCCATAATCCTATGGTACAAGAAGCT  
ATATGAATGGGGTTCAGTTTCAAAGACATTAAGAAAATAATGGAGGAAAA  
AATTCAGACATCTGGGAGCAACTGTAAATCACTTGAGGTTCTGATTGCAG  
ATCCAGTGAAGGCTCAGAAAGACAGTACACAAGACGAATCAAGTCAGACT  
TCATTGCAGAAAGAGATTAGTACTGAAGAGCAGCTAAGACACCTGCAAGA  
GGAGAAGCTTTGCAAAATCTGTATGGATAGAAATATTGCTGTCTGTTTTTA  
TTCTTGTGGACATCCAGTCACTCGTAAACAATGTGCTGAAGTGGTTGAC  
AAATGTCTCAAGTGGTACGCAGTCATTACTTTCAAGCAAAAAAATTTTAT  
GTCTTAATCTAACGCTATAGTAGGCATATTATGTTTCGTATTATCCTGATT  
GAATGTGTGATGTGAAGTCACTTTAAGTAATCAGGATTGAATTCATTAG  
CATTTGGTACCAAGTAGGAAAAAATGTAAAGCCAGTGTCTTAGACACA  
GC

>Contig21

CGCTGTCTTAAGAACTGGGCTAGGAGTGAGCAGTGAGCCAAGATCGCACC

FIG. 4 (5 of 61)

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ATTGCACTTCAGCCTGGGCAACAAGAGCAAACTCCATCTCAAAAAATA  
CATATATATATATGACCCATAAAAAGGAGATAAATCAACACTTCAGAACT  
SACCCAACTTGCAAAGATACTATAATTAACAGAAAAGGACAGTTTACTA  
AGTACTCCGTATGTTCAACAAGTGAAAGATTAAACATATTAAGTAGAGAT  
GTAGAAGATATAAGAAGATCCAAAATGAACTTTATAGAGTTGAAAACTACA  
ATATTTAAGATAAAAAATACACTAGGTGGGATTAAAAGTAGATTACACATT  
GCTAAGATAAAAAAATGAGCCTGAATACAGCACAGTATAAACTATCT  
TAAACAAAAACACAGAGAGAAAAAATAACTTTAGAGACTTAGCTCTTATC  
CTCTATTTGTTTCTAAACAGAGGATAAGGGGCAGAAAAAATGTTTGAAGA  
AATCATGATTTTTTAAATTTCCAAGTGAATAGGAATAGCACTGGGTAGTC  
ACAGGAGGCTGGAAAGACCCAAACAGCAGTTAAACAGGAACTAGGCAAA  
GAAACCAAAGGATAACAGTAAACCTAACTAAGGGAGAGAAAACTGACAA  
AAGCTGACTTAGGATAACTGAC

>Contig22

CCTGAATATAAGCCGCAAGTAACCAATTAAATTTGTTTTCCAAAATTGTA  
TTAACAATCTATGAAATTTTTATCTTGACCATAGCTATAACTCCAGAAG  
CCTTTTATAACCTCTATAACCTTTATTAAGGAGTAGGTTAATGCTTCAAG  
AAAACTTGTTAATCTGACACAGGACCCATATGCTGATCTTGCATCAGTG  
TGGCTTGGACATCAATGATTATGATTAATTTATAGAGAAATTGAACCTTAT  
TTTATCTCTCAAAATTGGCCCTTACAATCTCACACACCCACCTCTCCAC  
TATAGTTCCCTGGGCCTTGAGTTGAATAGCTTTAATTTCTGGCTCTGTGT  
TCAAGAATGCAGTTTATTTTGATTGGCATTCTTACCAGTCTGAAGATG  
AACCTTTAATGCTGTGTCAGTATTTAAGATTTAGCAGGACTTGTCTTTTA  
AGAACCAGGAGTCAAGCCCTATAACTCAATGTCACAAGGACTTTAAAAGC  
ACATACATAAAGATATATGGATGTAATAATCATAATTTTTAAAAAATTGT  
ATTAATCTCAGTGTCTTCTAAGCAAAACCAAACTTAATAATAATGGCATA  
GAAATTATTTCAATAAAACATAAAATCTGTTAAGCCAGTTACCAAAAGGC  
AAAAGAAAAGACCTTCTGCAATGCACAGAATATTATGTTGGAAGAAAACA  
TTTCTTTAGACCTTTAAGAAAACATTGTTAGCATCAGGACACAACAAAC  
AGAATCTGAGGTTAAGAAAACGTATATGAGCTGAAGGGAGTTGAAGGAGGG  
CATTACTATTTCCACCCCTTTTAAAGGGGAGAGAAAACCTAAAACAGCAA  
GATGCAATAAAAGCTGAACCTTTGGGTTAAAAAAAATTCTTAAGTCTCTT  
ATAATTTATTAAGAGTGAATCAACCCCGTAAGAAAATTTCAATGTTCTAA  
CCAAATTTTTAATATATAAGTAGTTTTTAAACATCAACCCAATCTCTAGA  
AAGACCATTATAATTTCCCTTTAATTATAGACAACCTTTATCATATAAAG  
TTTTTTAAATAAACTCTCTTATTGTGACTTACACAGACTATTATGACA  
TGCTTGGACTTTCTGGTTTGTGTCGTGAACATCCTTTCTTTCTTTCTT  
TTTTTAAATTTTACTTTACGTTCTGGGATACATGTGAAGAATGAGGT  
TTATTACGTAGGTGTACATGTGCCATGGTGGTTGCTGCACCCATTAAAC  
CGTCATCTATATTAGGTATTTTCTTAATGTTATCCCTCCCTTGCCCCC  
CACCTCCTGACAGGCCCTGGTGTGGGACATCCCTCCCTGTGTCCATGTG  
TTCTCAATGTTCACTCCCACTTATGATTGAGAACTGCAGTGTGTTTT  
CTGTTC

>Contig23

GCTAAATATAAGCTATGATAAAACAGTTGGCCCTCTGTATCATGGGTTTC  
ACAACCTGTGGATTCAACTAACTGTGGATGAAAAATCTTGGGAAAAAAG  
AATGGCTGCATCTGTACTGCACAAGTGCGTGCTTTTATTCTCGTCATTAT  
TCCCTAAGCAATACAATATAACAATTTTATATAGCATTACGCTGTAT  
TAGGTATTATAAGTAATCTAGAGATGATTTGAAGTATACAGGAGGATGTG  
CTTAGGTTACATGCAATATTATGCCACTTTATATAAGGCCCTTGAGCCT  
CCTCAGATTTTGGTATCCATGGCAGTCTGGAGTCAATTCTCCTGCAACA  
TCTCCATTTGTTGAGATTCTCTTATATCATGTTTATATCAGAAAATCT  
ACATAAGATTTTTTAAATGTGTTTATATAGGTTTTGTGATTTTTGGTGT  
TAATCCCTAGATATATGCAGTATTTATTGCTATTATGAGTAGTGTCTT  
TACCATGTATTCTAGTTGGTTATTGCTGACAGAGAAATGTTGCTGGTGT  
TCTAAGTTACCTTGTCTTAAACACCTTGCTGAACTCTTATTAGTCTCA  
TAGTTTTTAAATTAATCTTTCTTAGTTCTGATAACATAATCTGCAATAAT  
TCCCAAAGTATTTCCAGGATCTCCACTATAACATTAAATAGTAATAAGA  
ATTTCTGTCTTGTACTGATCTTAAGGAGAATAAATTTAAATTTCTCTG

FIG. 4 (6 of 61)

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TCAGGTTTTATGCTTGATATAGATTTGTGATATATAGCCTTTACAGGT  
AAAAAAAATGCTTTCCTAGTAGTCCTAATTTTTTAAAAAATCATCATA  
AATAGATGTTGAACATTATCAAATGCTTTTTCTGCATCTATAGAGATAAT  
CATATGGTTTTTTTACTATTTATTAATGTAATGAATTAGACCAATTTCTA  
ATGCCAACTCTTTCTTGATTTGTAGGGTAAATCCTATGGGATCATAAAA  
TACTTTTAATACATTGTTAGATTTGAAGAGTTAACGCCTTATTTAGAACG  
TTTTTCAGTCACATCCATAAGTGAAATGGCACTATAGTGTCTATTACTATT  
ATATTTTTCTGGTTCTGAAACCAAATTATACTCACCTCATACAGTAAGT  
TGGGCAACTTTTGTCTTTTTTTCTGAAACAATTTGTGTATAGAAGAAAT  
TAACTGTTCCCTGAAAGTTTGATAATAATCATCCAGAAAATTATCCCCAT  
CTAGGGCTTTTACAAAAGGAGACTCTAGAATGCCATTTTCGGTTTCCTTG  
ATGTGTATTGGCCTCTTTCAATTAGGCTTTTGGATTTTTTAGGGCATTTT  
TTCATATAGGCTTTTTTACCGG

>Contig24

CATAAACTTCAGGTTGGATGTTTCGGTCAAAGTGGTCCGGCGATGCGAAAA  
CGAGAGGGCTCGAGGACTGGGCAGAGAACTATTTGAAGGTATCTCTCAGG  
GGAAACCAAGCGGAAGGCGGGAGTAAATTGGGAGGGAGCGACGGCCTT  
CAAAGAAGGGGCTTGCAATTAGATCGGCGAGATCCGGGAGGGTCTGGTGGG  
GAGAAATGACTAGAGGACAAATCTAATGGAGAGACAGACGGAGATAGATA  
TCGTGACAGAGAGAGGGACAGTGACAGCGCACACAGTGCAGGGTCCATG  
AGTACAAGGCCCTTAAGTGTACACCCAGCCGGAGTCATGGCAATTCGAT  
TCCTGTACTGACCACCCAGGATTTGGGTAGACTGTACGAGTTAATGAGCA  
TGGTCCCCAACAAGACTGCTTCGACCTCAGATGCAAAGCACACTTCAGGG  
GTCCCCAAGCCACTCATGTTTTTTGAATGACTGCCATAAGTTCAAAAATT  
CCCACAATTCTCTCAGATTCAATAACTGGGTATAACCACTCATAGAATC  
AAGAAAATGCTATCATTATTATTACAATTTTATTATAAAGGATACAAATC  
AGAAGGACTAGCCAAATGAGGAGACACATAGAGAGAGGACTAGTAAAAAA  
CAGAGCTTCTGCGTCTACCTTCAAGGAATCAGGATGCACCACCTCCCA  
GCACATCAAGTGCTCATCAACCAGGAAGTTCCTCTGAGCTCCAATGTCCA  
GAGATTTTAGGGAGGATTATTACATAGGTATCATTGATTAAATCATTGG  
CCATGTACTTGAATCAATCTCCAGTGTCCCTCTTCTCCCTAGAGGTCTG  
AAGGGTTGGCTAATCATGTGGCTCAAAGCCCCAACTCTAATTACCTTT  
TTGGTCTTTTCAGGGACTAGACCCCATCCTGAAGCTATCTACAGGCCCTG  
CCATGAGTTAGCTCATTAACATAACAAAGACACTTATATTACTCAGAAAA  
TTCCAACAGTTTTTAGAAGCTCCATGTCAGGAACCTGGGACATAGATCAAA  
TTCTTTTTTTTTTTTTTTTTTTGGAGACAGGGTCTTGCTGTGTGCCCAG  
GCTAGAGTGCAACGACAGATCACAGCTCAATGCAGCTTCAACTTCCCAGG  
CTTAAGTGACCTTCCACCTTAACCTTCCAAGTATCTGGGACCACAGAAA  
ATGGCTAATTATCCTGGCTGATTTTTTAACTTTTTTTTTTTGTAGGGATG  
GGATCGCCCTGTGTGCGCAAGGTTGGTCTCAAACCTCTGGGTTCAAGCAA  
TCATTCTGCCCTGGCCTCTGTGATGGTTAATACTGAGTGTCAACTTGATT  
GGATTGAAGGATACAAAATAATTTTTTGGGTGTGTCTGTGAAGGTTTCG  
CCAAAAGACATTACTTTGAGTCAGTGGACGGGAAATCCCCCTTCCCCA  
TGGGACGGGAGACCCCCCTCCATCCAGGTAAAAAAATCTAATCACCTGC  
AATGTGGCAGAAATAAAGGAGGGAAAAAACGGGACCCCTANATGGGTTA  
TTCTCCACCTAATCTTCCCCCAGG

>Contig25

CCATGTATTTTCAATTTCTACAGACCCTGAGATGAATTTGTCAATTGCCACGG  
GGTCTGAAGTTCAAATACTCTATTTGGTATCCTGCCCCTGTGGTTAACT  
GTGATCATTTCACTCACCTTGTTTATGATGAGAGGTGCCACCATCTGGCC  
TCCTCCACTCTGCAATCCTGTTAATTCCTATCAAAGCTGAAAACCTGCTG  
CAGCACCCACACCATCACCTCCAGCCTAGAGAGGGGAAGCTACCAAGTGAGC  
TCTCCTGGATGCCGGTGTGCCCTCGCCAATACATTTCTTCTTAGTCCCT  
TGGTCATCCTGAGGTGTGTGATTAATGGACAGCTATGTGGATTGCACATA  
ATAGATGTATCCAGCATCTTCATCCCTGATTTTCTTTTACAGAAATCAC  
TCAACCTTAGCAACATGTGAAAATCACCTAAGGACATTCTTTAAATCCCT  
CTGTCCACATGGCAACACAAACCACTTAAATAAGAATCTCCAGGGAGTCA  
CTCAAGCATCAATGTTTTTTTAAAGCTCCAATTTTAAGGATCATTACATTA  
TGTCGAAGAAATTATAGTATTTTACGCTTACTGACTGTAAACCACCACCA  
TATCTAAGCATCCATTAGTCAACCTAGCAGACAATAAACTAACATTACCT

CCAGGTACTCAAATCAATTCATTGTCATCCCAAATCCCAGATGGGCCACC  
CTTATTGACAAATTCAGCCCAATCTTGGTTGAACACATTTAGAATATATT  
TCCATGAACAATATCCGGTTGACGAGTTTCTTTAACTTTTGGAGTTTAA  
GCCATTTCTTTTACAGTAGCCTTGTTAATTCCCTGTCAATGCTCCATGG  
GGGTCAATGAAGAGACCTCTTATTAAGTGTGAAGCAACTTGGCTCAGGTGC  
AGACACTCAAATGCTTCACATGCAGTGGGAAAAGAGAGTGATTGTCTAC

>Contig26

TTTAAAAAGAACTGAGTCTTTATTTCAGTCGATTCTTCTAATCTATGAACA  
TAGCATCTCTCTCAAAGCATTTAGTCCTTCTTTAATTTCTGTCAATTAAT  
TTTTAAATTTTTCATCCTAAAGATTCTGTATATGTTTTGTTGAATTTATG  
CTTAAGCATTTCACCTTCTTGGTAACAATTATAAATGATTTTGTGTTTTT  
TATTCCACTAGTTTCATTTTCAGTGTGTAGAAAAGCAATGAATTTTGTGT  
GTTGATCTTTGTTCCAACATCTTGAACATTATTGAACTCATTATTAGT  
TCTAGGAGGTTTTTTCATTTTTCTTGTAGATACCTTGAGATTTTCTATAT  
AGACAGTCATGTTGTCTGCAAACAGGCACAGTTTTATTCTTCTTTTCA  
ATCTATATGCCTTTTTTTTTTTTTTGCCTTATTGCAGTGGGTAGAACTT  
CTAGCACTATGTCAAATAGCATTGGTGAAAGCAGACATCCTTGTTCCTTG  
TCTTAGAGGAACATTTGGTCTTTAATCTTGATTTAAAAAATCCTTGCAC  
TAAGTTACCGTGTTTTGGGGAGGGAGAGGTGGGGTGAGGTGGGGATTTC  
CCCTAATGTTTACAAGCTGGGATTTTTCTTTTCTGTGTCTAATTATTTT  
CCTCATTTGGCTTGAAAAATCTGATAAAACATTTTAGGACTGTGTATAAAA  
TAGAATTAGCCAAGTGCAATGTCTTTATTGAGAAGAAATTTTCATGGACGT  
TGTGCCTACTCTCTTGGCTTCTTGGCTTCATGGCTTTCCAGATCCACAG  
TAAGCTCTGGATAGTAGAAGTTATAGTAAGACTGACTTCTAAATAAATGA  
AGTGACTTTAACCTTACTGATATGGCTTAAAGAAAAGGAGTGGCCTTTAA  
GATCCATGAACCTTCTCAAACAAAAGTGATAACGTTATCTCCATGCATATA  
TAATACTAAATATAATGCAACTGAGAGAAGTAGGCTGTGGTAAGAAAGGA  
GACCCAAGTGCCATCTGAAGGCAGCACTTACCCTCTGCTTCATCCCACC  
GAGGAAACAAAGCATGAGTATTGCCAGATTTTCTTCTGTTTCAAGAAAAG  
CCAGAAATCCAGGTTTTTGGCGTAAATGTCCTGATTTTAAATGTTGGGAAC  
TAATTTATATTTTGAATAACATTGTGTGGGACAAGTGAACCTGTATGTG  
GAACTGCTTTTCTCCAGTGGCGACCAGTTTGGACCGTTGATACTCAGCAA  
GTTTCAGCCAAGTGCGCCTTGTCTATTGTCAGTCATCAAGGTGATGTGTGAT  
TGGTCAAGCAATTAATTTTGTCTCAGCATCTCGTGTGTTTTCAAAGAAGT  
GAAGGTTCAATTTGC

>Contig27

TTTCAGAGCACAATGCGTATTTCATAGTATATTGACTTAATTTCTAAGTGT  
AAGTGAATTAATCATCTGAATTTTTTATTTTCAGATAGGCTTAACAAATA  
GAACATCTGTATATAAATGTGTAAATTAGAGTTAATCTTTCCAATCACA  
TAATTCGTTTTATGTGAAAAGGAATGAACCTGTTCCATGCTGGTGGAAAG  
ATAGAGATTATTTTAGAGGTTTGTCTGTGTTTTGGGATTCTGTTTTT  
TTTTAAATTTGAAATATGTACTTGTGTGAATGATTTTTTAAATGATTT  
TACCATTTTTGGAAGGGTATTAAATGATAGAATATCATCGAGCCAACATG  
CACTGACATAGAAAGATGTCAAAGATATATTAAGTGTAAATGCAAGAGG  
GAAAACACTATGTACAGTCTGAGCCAAATCAAAGCATGTATGTTTTTAT  
ATGTGTACAACAAAAGGTTTGGAAAGATATGCGCCGAATTGTTAAATGTG  
GTTTCACCTTGAGGGGGTGGGAGGATGGGGCCCCAGAGGGGTTTTATGGG  
GGCCTTTCACTTGGTATTTTTTTCATTTTGTCTGTTTGAAATTTGTTT  
TTTCTTTTTAAATGGAGTTTCACTCTTGTGCGCTAGGCTGCAATGTAGTG  
GCGTGAACCTCAGCTCACTGCAACCTCCGCCTCCAGGTTCAAGTGATTCT  
CCTGCGCTCAGCCTCCCATGCTCCTGTGTAGCTGGGATTACAGGCACCCA  
TCACCATGCTGGCTAATTTTTGTATTTTTCAGTAGAGATGGGGTTTCACC  
ATGTTGGCCAGGCTGGTCTGTAAATTCCTGACCTCAAGTGATCCACCCACC  
TTGGCCTCCCAAAGTGCTGGGATTTTCAAGGTGTGAGCCACCACGCCCAGCC  
CTGTTTAAATTTTTATAAGTATGTACTACTTTTGTAAATCAGAATTATTA  
GAAAGCATTTTACTGATTTAAAAGCTTAGACATGTTCAAATGCCTGCAA  
ACTACTTAACACTCAGCTTTAGTTTTTCTAATCCAAAAAGGCCGGGCAGT  
TAATCTTTTTTGGTGCCAATGTGAAATTTAAACGGTTTTATGTTTTTCTG  
TGTTGTGAATGAAAAATATTTCTGAGTGGTGGTTTTTGTACAGGTAGACC  
ATGCTCTGTCTTGTTCAAAATAAGTATTTCTGATTTTGTAAATGAAAT

FIG. 4 (8 of 61)

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ATACAATATGTCACAGATCTTCCAATTAAGTAGTAAGGGTTTATCCTTAA  
TCCTTGCTAATTTAAGCTTGCATAAGTCACTTTACTAAAAGATCTTTGTT  
AAGCTAGTATTTTAAACATCTGTCAGCTTATGTAGGTAAAAGTAGAAGCA  
TGTTTGTACACTGTTGTAGTTATAGTGACAGCTTCCATGTTGAGGTTCT  
CATATCACCTTGTATCTTGAAGTTTCATGTGAGTTTTACCATTAGGATG  
ATTAAGATGTATATAGGACAAAATATTAAGTCTTCTTTTACCTAAGTTT  
GCTTCTTGACTAGTAATAGTAGATATTTCTGTAATAAATGTTCTCT  
CAAGATCCTTAAATCTCTTGGAAATTATAAAATTATTGGAAAGACAAGA  
ACAGTTTTTTATTTCATTATATGCATTATTATCG

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CTTTCTCAAGAAAAGGGAAGTGGAGCAATTAACATATGTAATTTTTTTT  
TAAAAACCTTAAACCTAAACATCTACCTATATACAAAATTAATTAACA  
ATGGATCATGGACTCCAATGTAAAACATGAAACTCTAAACTTCTAGAAAA  
AAAACCTGGAGAAAACCTTTGGTACCTATGACAAGGCACAGTTTTTAGACT  
TAACACTAGAAGTGTGAACATAACAAGAAAAATTAATAATTTGAACCTT  
ATGAAATCAAATTATTTGCTCTCCAAAAGACCTGTTAAGAGGATGAAA  
ACTAAATTACAGATTGAGAGAAAAATATTTGTAAATCACATATTTGACAAT  
GGACTTGTATCTAAAATATCTAAAGAACTCTCAAACTCAACATTAAAAA  
AAATATCTAATTAGAAAATGAGTGAACATTTTACGAAAGGGCCTTATAG  
ATTAGCAAATAAAACACTTGAAAAGATACTCAGCATCACTAGCCATTAGA  
AAAATGCATATTAACCACAATAATGTATCGCTACACACATATAAGAAT  
GGTTTATGAAAAAATAGTGATGACACCAACTGTTAGTGAAGATGTGGAGA  
AACACTCATACATTGCTGGTAGAAATGTAAATGGCATAGCCACTGTGGA  
AAATTATTTGGCAGTTTCTTTTAAACTAAAAATCAATCTACCACACAAC  
CCAGCAATTTTATTACAGGGCATATATCCCAGAGAAATGAAGATTTATGA  
TCACACAAAATCTGTACACAAATGTTTTATGGTCACTTTATTTCATAATA  
GCCAAAACCTGGAAACTATCCAAATGTCTTCAATGGGCAAAGGATTAAA  
CACACTGTGATACATCCATACCATGGAATACTACTCAGCAATAATAAGGA  
AAGAATTACTGCTACACACAAGTTGGATTAACTCAAGGAAATTTGTGCTG  
AGTGAAAAATTAACAAGCCAATCTCAAAGGACACATACTTCATGATTCCA  
TTTGTATAACATTAATTAACACAATTAATTACAGAGATGGAGAACAGAAT  
AGTGGTTGCCAGGGATTATACATGGTGGACGCGGTGAGGCGGGCCTCCAC  
GCCTTGGAGATGAAGGGGGCTACACCTTTTAAAGCACACCCACGAGAGAG  
TTTTGTGCGGAGGGGGCCCAATTTAAGTACTCCGCCCCGGGGGGGAACAC  
AGGGGCAAACAAAAAAATTTGGCCTTGGGGGTGACCAACACACAAAAA  
AAAACAAACACACAAAAAAACAACNATGGGTGGGAGGATTAATCGCCAAA  
TCTGAGTAAGCTATCTGGACAGTACCAATATCGATTTCCAGTTTTGATG  
TTGTACTATAATAATGAAGATGTTAACAATTGGAAGAAGCTGGCTGAAGG  
GGGCTCAGGAACCTCTCTGGACATTTCTTTGTACCTTCTGTGAATCCATC  
ATTATTACAAAATAGGACATTTTCTAAAGGTTAAATCATTTTAAATTTTAA  
AATGTCCCTGTTACTGTTGAAACTCACATCTCCATATACTGATCAAGAAC  
AGCACTAATGGCCCCCTGGCCTCCAGGAATTCACAAATCTTACTGACTTTT  
CTTTGAAACCTTGGCCAAGTCGCTTCTCTCTCTGGTCCCTCAATTTTTCA  
TCTTCAAAATGAAGATTGAATGACTATTAATCTCTTGCAATTTCTTGAG  
ATGAAGGGTCTTAAAGGAACTGAAGAGGATGCCATGTAATGTAAATATGG  
GTTTTTACTCCATCAGCCAGCCAAGACAGAGGGCAGACACCAAGACATGG  
TAACCAAGGAGGCCATGTGTAAACAAAGACCATTTAGACTTATGCTCTGG  
CCTTTGCAGCCCAACTGGTGTGGCCAGTTGGTGGGTATGAAGAAAATGG  
GGCCTTCCAGGAACCATGTTGAGTGGAGATAAGCAGGGAGGAATGCAGAA  
GACATGGGGGCAGTGCCAGTCTCAGCCCCAGCCAGCTACACCCACACATG  
GTTATGAAAGACTGACAGCCTGTAAGNTGAACACAGCCCTGCCTCTCTTA  
GATAGGC

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GCAAAATATGATCTCAGATGTGGATTTACTGTAAAGTTCATCAAATTTAAA  
TTTCAGAACACTTAATCTGCAAGAGTCCTTTCCAAGACCTTATACCTAAT  
TTTGTGTTTACAATTTTATATTTGTTTTCTTAAAGAAGACCACCAATATA  
AACTATATCCAGCCTTCATGATAAGTACATAGGAACTATGCAAAATAGG  
GGGAAAAAAAACAAAGAAAAATACCTAGTTTACTAATGGTTCACTTCTGA  
ATAGCACATATTATAATGATACAAGCACTCATTACTAGTCTAGGAAAAAT  
GAAGATATAATTGCATTAGGAAGATCAAGAGGTAGGAAATGTGGATGTGT

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GTGGTATAGACTAGGGCAGGACAAAGAACCTAAATCCTCATTTTCTAAAG  
ATAATTGTTAATACGTAAAACTCAAAATTCAAGAAGTAACAGTAAAAGCG  
GTCATTAAAGAAACAAGCACTAAACACCAGATAGGAAGCGAGAGATGGGGG  
AAGAGGGGCGACAATCTGATTATTTTTTGCAACAAATTTTGTAACCATT  
TGACTGTTTACATGTAGAACTTGGATCTTTTTAAAAAACACAAAATAAT  
AATACTATTATTTTTAACTGGATTTTGAAAAAGAAGATAAAAGTCTCA  
TTTTAGTAATTAACACTCATTCCAGGTTAGTCCACTCAAACTTATATTC  
GAAAATTAACACTTTGGGAGGCTGAGGCAGGCAGATCACCTGAGGTTGGG  
AGTTTCGAGACCAGCCTGACCAACACGAGAAACCCCGTCTCTACTAAAAA  
TACAAAATTAGCTGGGCGTTGTGCATGCCTGTAATCCAGCTACTCGGGA  
GGCTGAGGCAGGAGAAATTGCTTGAACCCGGGAGGCAGAGGTTGCAGTGAG  
CCGAGATCACACCATTGCACTCCAGCCTGGGCAACAAGAGTGAACTCCA  
TCTCAAAAAAAAAAAAAAAAAAAATTAACCTCTGGAAGTTGAGTTTG  
CAAAATTCATTATGCTATTTTAACTTGTATGTTTGGAAAATGTCATG  
ATGAAAATTGAGGTTGGGGGATGAGAAAAAAGAAAAACATCAACCCAC  
AGCCCATTCATTTTCAGCCCGACCCACAGCTCCGGGGAAGGCGAGCAGG  
TCCATCCTTCACTCTTTCTTCACTCTTTCCCTCCTTCTGGCTCTTCCA  
CCTCTAATTTGGAGCCCAAAAAAGGCACTGGGAAATGGAAAAGTCTTTT  
GTACGTGGTACTTGCCGGGGAAGCTGCCATGAAAACCTGGCCCCACGGTG  
GGGAGGGAATGCCANCTGAGGCCTCGTGCCCATGCTAGGATAGACTCGT  
CCAAACATGTCAAGTGGTCTGACAGGGCAAGCANCANGAAATCATGTATG  
AGTATGAAGTATCTGTATGCAAGGGCGGGGAGAACACGCGGAGGAATGG  
GGCGTGAGAAAACAGCACAGTACGTTTCTTTAGCAGCTGTCTCTGCTCAG  
CCATGGGAGGTCACAGAGAAAGAGGCTTGGAGGCGTTATTTTCACTGTGA  
GATGTGAGTGTAAGAAAGTGCCCAAGACACAGTGAGTACCAGGGAGATGC  
CCTCTTTCTACCCGAATGCAGAATGGCCACAGGCCTTAAACACACACA  
TGGGTCTCTCAGAGGAGAGAGGCCTCCACAGTGGACACCCGCATTCTCCCC  
TGGTCAGCAGCAGCAGGGCGAGTGCTGGGCCATCATGAAGCTTCACAGGC  
AATGAGCTCTCAGCAATAACAGGAACAGTGCCTGGGGGACTGTAGCTGCA  
AGACCGATTTTCATGTAAGATGGCCTCTGAGGACTCCGAGATACACCAGG  
CTGAGACTAGCTGGCAGCTCCAAGTTGTTGGTCAGAAGAGAACAGGAAC  
AGGGAAATTGGAATTACTGTTACTACAATTCCTTTACATCCGCACAACCA  
TGAGGTCAGCGATTTTCTATTATTTTTTTTTTTAAGACAGGGTCTCAGT  
ATGTGCCCCAGCATAGAGTGCAATTGATGTGATCATGGTTCACTACAGTAT  
TCAGTCTCCAGGCTCAAGTGACCTCCTGCCTCAGCCTCTCAAGTGGCTG  
GGACAGCAGTTGCATGCTACCAGGCCAGGCTTTTTTTTTTTTTTTTTTTA  
GTTTCTGTAGACCATAGC

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GGTTAACAATGGCACAGGGAAACAAACAGTTCAGGTGCAGGGGCTCTAA  
ATCTATCATAAGATGTTAGGTATGGGGGCTCTGCCGGACACAAACTCAAG  
GCTTTATGCTGTTATCTCTTGAGCGAAATCCTGGGAACTTCGTACATTGC  
TTGCTTCAGTACCTTATCAGTTAATCGGACTCTTTGATATGTTGGGAGTC  
AGCGTACACAAGTTAACTCCTTGAGGAAGGGGGTGGGTAAGGAGTCCTTG  
ATGTCTGGTAAATGAAGGAGCGAAATCGAGTTCCTCTGGCTTTCTCAGCT  
AAGGGAGAGCTTATTATGTGGAAACAAGGCTAAGTGATTAAGGGAGAAA  
GGGAGAGTCTGAAAACAAGGTTAGGTATTACAATGTCAATAAAATTGGTC  
TCCTTATACAGTCTATGGTAGATTCTTTCCATCTTTAATCTCCCTCTA  
GCACCACCAGACTTTTTCTCTGTACCTTGAGATGTAAATTTTGCTATC  
TGAATTTTCGTCTAAGAGTTGTTTCCTTTAATATGCAATTTAGGGTTAT  
TTAGCTGACAACTGCCAAAGTAGTGAACAAGTTATCAAGAACTTGAACG  
TCTAAGGTAGGAAAAAAAAAAGTCTTTATGAATCTATAAGATGTACTTCT  
ATTGGCATGCCTAATACGTCTATGTATTTACGTGTTGTGTACACAGTTTT  
TCACTACTGAAAATATATAGAGGAGTTCTAATTAATTGACTTAAGACAAT  
AAAAGCGCTTGAATCAAATACCTTATCAGGAAAAAGGAAAAGACAAGTCA  
AATGCTTGTTCAAGTTTATATAACTTAAGTAAATCTTTAATAAATAAGC  
TAGCTTTAACATTATTTGAAATGTCTTAAGAATTGCCAGCAGGTTCTGGG  
TTACAGAACTAGTGGGGGTGCACTGGGGTGAGGGTTGGTGGGGTGGGGG  
TGGTACGGGGGCTTTGTTTTTTCTTGCTGCCCCCTTCTGGGTGGGGGAAG  
TGGCAGGACCTTGGCAGCACCCGAGCCGGCATGGCGTTAATAATGGAGG  
GATGCCAGACCCAAGTGGCTAAGGCCCGGCTGCAGAGCCAAGTTGGCATT

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CTAAATTTTGTAGTGAGAACTTGAGCTTGCTTCTGTGAGATATTTATTTT  
AAAAAGATTTTGACACTTTAAATGTCTAATCAAGCCTTTTAAACCATGAT  
CTATCTCTTCAAATTTCTTCAGATGCCACCATCAATAAAGAAACTTTGTTC  
ACACAAGTAAGTGGTAGCAAATGGCAGGGTGTATTATCATTTTTTTTTTTT  
CTTTTTTTTGAGACGGAGTCTCGCTCTGTGCGCCAGGCTGGAGTGCAGTGG  
CGCGATCTCAGCTCACTGCAAGTTCACCTGCTGGGTTACGCCCTTCTC  
CTGCTCAGCCTCCCGAGTAGCTGGGAGTACAGGCACCTGCCACACGCC  
CGGCTAATTTTTTGTATTTTTTAGTAGAGACGGGTTTCACCGTGTTAGCC  
AGGATGGTCTCGATCTCTGACCTCGTGATCCGCGCCCGCTCGGCCTCCCA  
AAGTGCTGGGATGACAGGCGTGAGCCACCGCGCCCCCGCGTGTATTATCA  
TTTTTGGCTGATGAAATTTTCTTGCCACTACTCTGGATGGTTTGATAC  
ATTTAAATTGTGCTTCCAGGGTACAATTATCCTTTAAATCTATACCTCTT  
TCCTTTCTTTTATTGACAAATATAATGTTACACTTTTCTGTCAATGACAGC  
CACACCACCAGTACACAGATCCCAACAGAGTTGTAATATTTTATTAGTTT  
CAGAGTTTCAATATTTTATCACTTTCAATACTTCATGTGCAGGAGTTTTA  
TTTGGTACTTCTTTACAAAATAAATGATGTCTTCCAAGCATTTCTTTT  
AATAATTTCCAATCAATGTTTATTAAGTAGTAATACTAGTATCTGTTTATT  
CATAAATTACAGGAAATGCTTTTTTACTTATTAGTCTTTGGAATTCTGT  
TGTTTGTATAAACATCTTTCATGATGGCTTTGTGTCTACCAATAGCACTA  
TTGCCAAAAGGCACCTTTTTCTGTTCCTTTACTTCACTGGTCCGAAGCC  
TGGTACCAACAACTACCACACAGACTGGGAAATGAGCAATTTTGCCACGT  
GCCCTTAGCTATTAATGGTGGCACTCCATAACTAGCATCTTAAGCTCAAT  
TTCATGAAAGAAATGTGTTTCTTATTTTGTACTTGCAAGGCATTTTAA  
CTTGTAATCTTTTATTCTACTTTTAAATTTAAACAGAGTAATAGAACC  
ATAGAAGGAAATCAATACCCACGAGTCCATACTGATATAAAATAAATAGTT  
ACATAAATAAATGGGGGGAGAAATAACAGCTCTTCTTACAGAAAAATTT  
CAATTAATAAATGAAGAAGGAATTAGGGAATACAACGTTACCATTAAGC  
AACCACAGTAATAATCATTACAGGCAATATCCAAAAATAAATCCAAAGC  
CAGTGGGCAAAAGTTTTGAGGAGATACAGGATATTAACATAGTCTCAAAT  
AGCTCATGTCTATTTATAAATTACAAAGGAACATAACACTGTATAGTG  
AAGAAACTGCGAGACACCACCTTAGCCAGTGATCAAGGTTAACGTCAC  
TAGTAATAGGCTTGTGACATACTGGACTCCAATCTGATACACTGATAA  
GGACATGACTTCTGCAGTATTCTTACCAAAACAGAATTCTAATGTAA  
TTAAGGAAATGTCAGACAAACCTATTCTGAGAAACATTCTATAAAACAA  
CTAACCAATACTTTCAAATTTGTCAAGGTCATAAAGACCAGGCGATGGTC  
ACAGATTTGAGGAGACTAAGGAGATACAACAATAACAAATGGAA  
CCATGGCATTCTTGATTGGATCTTGAACAGAAAAGGATATTAGGAAGA  
AAAGCTGATGAAATCTAATACATTCTGTAGTTTAAATTAATAGTATTGTA  
CCAATATTAATTTCTAGATTGATCATTATACTATGGTTAAGTTTTTAA  
CATTAGGAATCTGGGAGAATGGTATATATGAACTCCACTGTTCAATCA  
ACTTTTTCAAGTAACTATTATTTCAAATAAAGTT

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>Contig33  
GGGAGCGGGCGGCCACGCTGATCTCTAAAGCTTTAGACCACATTGGCTCG  
AGCATGGTCATGGCCGTTTCCTG

>Contig34

>Contig34  
GACGTCCTTAGCGCTATATTATAAAGAAATATTCACCTCCCTGCTGAGCTT  
ACAGGGGTGTAACCTAATGTCCAACAATATGAAATCTCTTCAATGAATTGCA  
GCACGTCATATATAGTCAACCCACATGGAAGCTGTCTCTTTCCTCACCTTCG  
AACTTCCCATTGCCAAAGAGGGGACCTCTTGGAAGTCAAATACATCTTAGCAA  
TATAGAAGATGCTGGAGACTTGTAGGAGAAGTGGAGAGGGTTTACAGTGT  
AGCCCCACAGAAAACAACTTATGACCCCATCAGTCACTTGTCCCTTTTTT  
CCATGCCTCAGTCTAGTCAGGAAACCACTAGATCCTGGATGGCTTCTTCT  
CCCTTCCCCTCCTTTCTCTTCTCCTCTCCCTCCCTTGCTCCTCCTTCCTC  
CATCACCCACTCCTTACTTCCAACCAAACTTGACTCCCTCCAGTCTCAT  
CCCTCCTTATTGAAAACATTTTACTCAGCCCTCCTCCCCCATCCTTGGC  
CAATCTTTATTCCTTACCTACATCAGACTTCACCAAAACAAAGGCCAGGA  
TAATAAACAGGACAAACTCTTTCAAACACATTTTAAATGACCATATTTTGT  
TATTTTGGTACAATTTGAGGAGTCCCAATCCCAGGGAAGACTAACAAGA  
AGTTCTCCTAACAAAGGTGGGTCTCCCTTACTAAAAACTCCTGTAATGG  
CTGAAAAGAGCATGAGGTTTTCTGCATATCATTACACATTCAATAGAACG

**FIG. 4 (12 of 61)**

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TCATGCAGCTGTTAAAAATGATCTGTAG. AGGCTATCTTGTGACAGAAAG  
 GCATTGGAGATATACTGTTAGTGACAAAAATAGGTTATAAATGAATTTTT  
 CCATGCATGCCTCTATATTTATAAATACACACACATAAAAGACAGGAAGG  
 ACAGACATTAAACATTATAGTGCTTAAGATGATGCATAGTATAATAGTT  
 AGGACCATGGCCTTTGGGACAGAAACTACAGCCTCTCTCCCACTTATCA  
 GCCATGGGACCTTGGGCAATTTGCTCAGCCTCAAAGCCCCCTGTTCTTTA  
 TCTGTGTGCTGGGGTTGTTGTAAGAGTTAAGTGCAATACACAGAGAGAGA  
 GAGAGTACCTAACATGTATTATGTGCTCAGTCAATATGCATCATAGTACT  
 CATTGTTACATATGTTCTTAAGTGCTTTATACGTTTTTTCCCTAAGTTGA  
 CCATCTGTTTTTTGGCATTATGAAACATAATGATCCTAACAAATTAAAATT  
 AAAAACATAAAGAATATTTGCCCAAAAAAATAAAGAACATGAATTCCTC  
 AAGTAGCCAAAGGGGCCATAGACAGAAGTAAGCCCTTGGTGGGGCTTAGTT  
 GAGAGAAGTCTCCAGAAGGTCTTTCGTGTGTTAAAGAAGAGGGTAACAGG  
 GAGGAGGTGGGGAGAGATGTTAACTGAGTCTAAATGAGCACCTGGAAGAA  
 GAGATGGGACAGGCCACTTCTGCCTGGACTCCCTGATTGTTAAGAAGAAT  
 GAAAAAGAGCAGAAGTCTTCCCTGAGCCCAACTTCACTCCCTGACTTAAC  
 CTAGTCTTTGCCCTTCCCTCTCACTCATGGCTACTTTCTGTGGTCACT  
 TGTGTAGAAATGGATGTGCAGCCACCTCATCTTTTTCTACCTCCTTCAC  
 ATGTTTTAGATAATTTAATGTAGTAGAAGACGGTTACAGCAAAAAATTAC  
 AAAAATCAAAATATCTCTGCTATCTACTGTTGCATTTCTAACCATCCCAA  
 AACAGTAGCTGAAAACAGCACTCGTGGTCGAGCGCGGTGACTCATGCCTT  
 TAATTCAGATACTCCGGAGGCTGAGGCAAGAGAATCACTTGAACCCGGA  
 AGGTGGAGTTGACGTGACTCAAGATCATGCCACTGCACTCCAGCCTGGG  
 TGACACAGTGAGACTCCGTCTCAAAAAAAAAAAAAAAAAAGCACTCGTG  
 TATTTTGTTCAGATCTGTGGTTTGGGCAGGGCAGGGCTCAATGAGGACA  
 TCTCGTCTCCGTTCCCGCAGTGTGAGGAAGTGTAAGTGAAGTGGAGGGT  
 CACACAGAAGATGGCTCCCTCAAGTGGCCAGCAAATTGGTGTCTACAATT  
 GACAGGGAGCTGTTGACCAAGGGCCCCAATTCCTCTTCCTATGGCCCCCT  
 CTCGGGCTGCATGGGCTTCTTTACAGAAATGGCAGCTGGATTCCAAGAGCA  
 AGTATCAACCTACAGAAGAGTGGAGGAATATTGAAAGTTCACAGTCTC  
 TTAAGACGTGGGCCAGAACTGGCAAAAGCTTCATTTCTGCCATGTTCT  
 ATTGATCAGTCACAGAACCTGCACCAATTCAAGAGGAGAACATATAGAGG  
 ACATCTCTCAATGGGATAAGTGTCAACAAATTTGCATCTATCACAATCTG  
 TCTTTTGGGTACAACTATTTCTATTCTCCTCATTATGCAAAATATACTCA  
 CAACCTCCCAAGGGGTGCAAAAGCCTCATCCATTTATGGCAAATGTGGCC  
 CTTTTAATTTATATAAAATAATTTGCGGGGGCTTCTTTATATTTTTAAC  
 TCCCCCTGC

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GTGCAGAGAAGTGATTTAAAGCCCTTCAGAAAGAATGCTTTATTCCCGTG  
 GAATTTGGTAACCTTGCTTGGGTGTGGGGAGGTTTGTGAGCTTTCTCCACT  
 CAAATTATCAGACCCTTTCCATTTAGTGGTAGACCATTTCCCTCGTCCAG  
 GCCAAGGGCACATAGTACAGAGAAATAGGGAGTTGTTACCCAGGGAGAGA  
 ACTTGGCTCTAAACCTGTAATAGAAAGGTGAGTTCTGGTCTGGAGGGTCA  
 ATTTTGATCTTTGGCTCAGATCCAGGAATTGGAACCAAGGCTTTTGAACA  
 TTTTAATGCAGGGGATTAAAAAATGATACGAGTCATTACGAATATATT  
 TGCTTAACATCTAAAGAGATCCCTCAAAACACTAGAAAAAATAAGAACAA  
 AAATCTAATAAAACAAAAATTTGTTAAACACATTTACCAAATTTTTTTTTT  
 TGGTAAAAATTCAAATGTCATAAATAAAGCTAAAGTTCCTCTTGATGACT  
 CGCTCCTCTGCCCTATTCCACTCCAAGTAACCACTATTATCAGTCTTGCC  
 AATACCTTCCAGACCTCTCTACCTCTATATACCATTAGAAGCACATGGT  
 TTTGCATTGAGGATGTGCAAGTGTGTTTTGTTTTACGTAATGTTATCACTCT  
 GTTCTTGTTCATAATTTGCCCTTTTTCTCTCAATGATTTGCTTGGCTATC  
 TTTCTATTTCAGTAGCATCTCCTTTCTTTTAACTTACCATTGTTTATTT  
 AACCTTGGCTCTATCAACAGATATGTAGGTTGTTTCTAGTTGATTTTCAAT  
 AAGTATTTATAAACAACGCATCAGTAGATGTCCATAAATTTCTTTACGGA  
 AGATGGCAAGTAGTGGAATTGCTGAGCCAAAGAACATGTTTAAAAAACCC  
 AAAAAAAGTAGACGCTACCAATTTTCTCTCCAAATGGCCATACCCACTT  
 ACCCATACAGAGATGATTTGGAATCTGGCTTCTCACAAGGTGAGATGCC  
 TTCACAGTTTCATTCTTCTGGCATGTCTCCCTTTTGTATCTGAGAGAG  
 CTGGCAGAATTGTGCTCAATAATCAAGGATAGAGGGTCAAATGACAGCTC

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AAGCTCACAGGACCTCTGCTTTCTTCLAGACCACCTGCTTTCTGCLA  
CCAGCTCTGTTCCATCTTATAGAATGGTTGCCACTTGGGTGTCTGCTCCG  
ACAGCCATGTCTATCCTTTGCACTGCAGTTATGAAGCAGACAGAGCTAGGA  
GAGGGGCTTTGCCAGCCTCTGCCCTAGCTTGGAGAACTTCAAAAAAGGAG  
GGTATTGAAGTTGAACTCCCCCAAAAGGGGTGGTCCCCACACCTCAAAA  
AGTGGTGCCTCCGAAAGAAATGTAAAATTCGTGTGGGGGGGAAAAAGGT  
TATTTAGAAATTGTTGGCTTGTCTGTGCCGAAAGTATGTGTGGTTACGGGG  
AGTACGGAAATTTGAGGGGTGGGGGCGAGGCCGTGTGTCTTTAGCCCCG  
GGGTTTTCCCGTCGCATGTTTAAGGGGGGGGAAGAGGGGGGATGTTTTCT  
TTCCGCGAAGGTTTTTGAAGAACGGCGTGG

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CCCCCACCAGGCACTACTCAACCGGCCGTTACGAAACAACCTCGCCACAT  
CCACTAACCCGCTGGCTCACCACCCACCGCCCTCCCGATCCCCCAATCC  
AAACTCAACCCCAACCAAGCGCCTCCCCCTCCCCACCCCTCCAGCT  
CAGCCCCAACCTACCACCAACCCCGACTCGCCACCGAAAAACCAACAGCA  
AACCCAAATGCCACAAAACCAAGTGTCCAAACCTCCTTCCCATCAGTTT  
GGTGGGCCCATCACCCTTCCCCCTGGCCAGGCTCTCCTTTTGTGCGCTT  
GGAGCAGCAGACTGATCTCCAGCCTTCACTCACTTCATGTGGTAATCTG  
TTGTGTTTCACTGTGCAATCTTCTGCATCCCCCTCACTACTCTGCTGA  
AAACACTCTAGTGGTCTCTATTGCTCATTATGAAAGTCTAGATATTAA  
ACGTAGAAGGCCCAGCACAATTTGCCCTATGCCACCTACCTCTCTAATC  
TTTTCTCCTTACTCTGACAGACTCTCCGTCTGTCAATTTATGTATTCTTT  
ATTGCTCTCTTCTACTTTTAGTATGAACTGGATTTATGGATTTTTTAAC  
ATTGCTTTCAAGTATGGAATAAAGAATTTTATTATTATTATTATTATT  
ATTTGAGACTGGGTCTCACTCTGTTGCCAGGCCAGAATGCAATGGTGCA  
GTCATATCTCACTGTAACCTCGAATTCCTAGGCTCAAGCCATCCTCCTGC  
CTCAGCCTCCTAAGTAGCTATGACTACGGGTGTGCATCACCACATCTGGC  
TAATGGAATAAAATATTACAATGCCTAATCTTAATTTTCAAAATTTTAA  
TTACATTGTACCTAATGCCCATGCATTTACTTTTTTTCAGTGGGTCAATAG  
CCCTCACTTTGGCAAAGGTCCCAGGCCCAAGGTAAGGCCCTTACTTTTTCC  
AAACTCATCTTTGAAAGACATAAGTGCCTGTAAGTTGTACCACATTAGG  
TTCTAGGAATTTTTCATCAAAGACTTTATCAGACTATTTTTCTCTAAGTT  
GAGAAAGAGCTGGGGGCAGAATATGGCACTGAATGACTGAAGAGAAGGCA  
CTGAAATCAGGCCAGAGGTTGCTGGAAAGAGCAATGAGGAACACCAGCAG  
CAATGAGGAGCCGGTGATGATTTTGGCTTACAGGGAGGTGTGTACCACA  
CCGATTTTATCTCTACGTGGATGAACCACAGCTGTGCGCTCCCTTGTCTC  
CAGGACATCACACTCTCCACATTCCCTCCCATCTTCCGGCTTCTGCTTCC  
CGGGGCCCTCATCTGCCCCATCCTGGGTGAACACTGGTGGTCAACTGCT  
GGGCGTACCTTCCCGCTCTGCACACCCTCCCTGGCCACCCCACTCTCT  
CACGGCTCGCACTGCAGAGGAGCCGCATCTCTAGCTCCAGCCCATCTGCC  
TCTTCTGAGCTCTAACTTCACTGATAGGCGACTCCTGCCGGTGTGCTCAC  
AGGCCCATCATACTTCAAAGCATTTTCCCCCTCAGAACCCATGTCTGGC  
TGCTCCCTCCAGAAGATACATCTCTCAAGCACATCCCCCGCGCTCTCACC  
TGGATGACTGCATTACCTTCTCCACATTGCCCCCTCCTTGGATGTA  
TATAGATTGTTTTAAATACAAATCTGATGTGCTTGTCTCCTGCTTGAA  
ACACCTCAAACTGCCTTCAAGATAAACCACTGCCCTTGACATGTTTACA  
GGTTGCCCATGGCCTGGCCCTGCCATCTCTTCAAGCTCATCTCATGCCC  
CTTGCCCCCTCGCTCTCTGGGCTTCTGCTCCCTAGCCCTCCTTAGGTTT  
TCTAACACACCATAGTCTTCTAGTGTGGGGCTCTGCAAGTGTCTGTTT  
CCATTGCTGAGACATGAATCCCTCTCCCTATCTCTACCTGCACCTTCAT  
CTGATTAATCCCTACCTTCTCTACTCATGATGTTGCTTTCTCAGGGACTC  
TCTCTGACTTTTTAACTAATCAGGGTCTCCCCAGTATATATCTTCATAG  
CACTCTGTATTACTCCTTTCTTAATGACCACCTGCTGTAGACAGAATGTT  
TGTCTTCTCCAAATCATATGTAAACCTTCCACCAGAGCGATGATTAG  
AGAAGCCTCCC

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GACTGACATTCAGAAGATATTAATAAGAGCACTAATGATGGGGATTGCAA  
CCATGTCTTTACTGACTTCCAGAAGCTTCTTACAGTAAACATGAAATCAC  
ATAATTTCTTCACTTTCTACTGTTTCTGTTCTGGGCTCTGTCTCTGCT  
TACTGTCTAATATCTTGGCCCCCTTAAAGTTGCTAATCTTCAAACTCA

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TTCTGTGACTGGGCCGCTGGTCCTTG...CATGGGCCTTGAAGATAC10A  
 CTGTACACTTATCTGGAGCATCCAGTGCCTACCACCTGACCCAGATTCCCT  
 CATTGCGCTCCTCCCTCCTCCACCTAATGGGATTGCTCATACCCGTGTG  
 GGACCCCTCCCATTTTCCCCAACTGAATACTTATCAAGACAACGCATTGC  
 CATACTCCCTCGTACCCTGCTCTGGGCATCAGACTGAATGTTTGTTCCTA  
 TTGAGGATCTGCAGCTGCATCAGTTTCCCCAGCACCGTCCAACCCCTTGA  
 GCATGGCTAGTCCTAAAGCAGAGAATTAGCCTTTCTATCCCTGCTGCTAT  
 ACATGCTGGGACAAATAATAAGAAATGACAGCATTTTATGATAATGCAGG  
 CTGCAGGAGGCAGGAGGCAGGAATCAAATTCGTGCTTATCAAATAGTGCT  
 CCAATTCCTTGAAATATTGGACTATAGAATATGTATGGATCTATGCTCAG  
 GTGGGTTCCTATTACTCACTCCACTGAGGCCAGGTTGTGGGATTAGCTG  
 TCCAAGAGGGAGTTTCAGTCTCACAGCATAGGGTCATTCTGAGAATTACT  
 GGCCCACTTGTGTGGAGACCTCCAGAGAACAGAATCTGGGTTGGTGCC  
 ATGTACTTCCAGGAGGAGAGAAGTGGCAGGATGCCAGCCCCACAATCAG  
 AGGGGAAGGGGCAGAGCCACATGTATGAAGATCCTCTCCCCAGTACGTGC  
 CAATCACAGGGCTTCCTAGCTTTTGGGCCAAGGAAACAATGTGGGAAGCA  
 AAAAAAGGACAAATTTCTCCTCCCTTTGCATGAAGACTGAGCAGTTTACC  
 AGATTCCTCAGGGAACACCCCTTCCACTCTGGGTTGAATGTGAGTGAGAGA  
 CATTGAGCTGGAACTACTAGAAAAACTATTTCTGAGCCACTCACCTTTAG  
 CCTAGAAAAGTGTGGATTTGTCTTCTATCTTTGCCACAGTAGAGACTGC  
 TGATAGCATCAGAACTTGGGCTCTGGAATTAGACAGATATGGGTACAAAT  
 CTGAGCTCTCTCATTATTAGTGTGGGATGTAGAGCAACTTTTAAATCC  
 TTCCAAACCTCAGACTTCTCATGCATGATGTGAGGATTGTAATAGGGCCC  
 ACCTAATAGGGGTTTTTGAAGATTAAAAAGTTATTCAATGAACAGCATT  
 TAGCAAGATGCCTGACCATTGAGAAAAATAACAAATTGTTTATTATTATG  
 TTATTATTAAAAACATCTTTCTGACCTTCTGACTGGGGGCATCGTATCAT  
 CAGAAATACTTAGGATGGGATGGATTCTGCATGGGCTGAGTCAAGGGTG  
 CAATAATGGAGGAGTGAAGAAGGAAGAAATGGAGGCAGAAATCCCCAGGA  
 GCCCAGCATGGTACAGGCTGAGCTAGTGTGCAGAGCCTCCTTGGAAACA  
 GCCACAGAGCTTGCATCTGGCCCTGGAGGAACCTCTTCTAGCTGGCAGGA  
 CCAGCCACAACAGTGGCCAGGGGATTTCCAGGGCGTGGGCTCCTCAGGA  
 GTTCATTGTGGACCAAGCCTGCCTGGAGAGGGGTTATAACAGGGATCCTTC  
 CCTACTGGCAGGTGATTTTACCCCTCGGTGAGAAGCTCAGGCATTGTTTG  
 ATGGAAGGTGGAAGGCCCTGTGCTGGGCCAGTACTATCAGGGATGGGCG  
 GGTGGCTGGAATAAGCAAATAAGACAATATGATAACACAGTTAACCACC  
 AACTATGTGAAGCTACAATATGGGTATCTGTAATAGACAATTCATGT  
 AGAGAATAATTTTAAAGGTGTCAATCTCCCCGCCAATGCCATAAGCACACG  
 GCCTCTGCCTGGGTTTCTCACTGTGGAATGTCTCCTGGTCTCCTCATGC  
 CCAGAGAGTGGGAAGTACTCCTACTTTAACACCGGCTTTCTGTCAATTC  
 CNTGCAGCCCTCCTCAGCCCCCTCTGCACAGGGAGGTTTCTCCTGCTG  
 CTGCAGTGCCTTCTGACTTTGTTAGTGGTACCTGCACACAGGTATTGGTGT  
 CTTGTCTCACCACCCTACATCACTGTAAGCTCCCCAGGAGCAGGCTTCCT  
 GTTTGACTCACCTGTGATCCTCCACCTCCCACCTGTAGTGCCTCAAGCA  
 TTCTGTAGAGCACATGGACGCC

>Contig38

GACTAATAAGTACTTCATTATTTGGGTATTTTCCAAGAACAACATATTGT  
 AGGAAACCATTCCTTTCTAAAAAAGTGTCTTTTAAAAAGGTGAATA  
 ATTTTGTCTAATTCAAAGTTTATTGAAAAGTTATGTATAAAACAAGGTA  
 AAAGGAACAAGGAAATAAGGGAAATGTAAAGAAAATTATAGAAAATAAAGT  
 GGTATTTTTTGGTAAGAAAGCTTAAAGAGAAATAATTTTAGGTAAGAAAG  
 AATCTTACCTAAAAATTTGTGCTAGAATAAAGTGACTGGCTAAGAAAGGG  
 ATGTTCAAAGCTATTTATGACAAACCCACAGCCAATATCATACTGAATGG  
 GCAAAAGCTGGAACATTCCCTTTGAGAACTGGCACAAGACAAGGATGTC  
 CTCTCTCACCCTCCTATTCAACATAGTATCGGAAGTTCTGGCCAGGGCA  
 ATCAAGCAAGAGAAAGAAATAAAGGGTATTCAAATAGGAAGAGAGGAAGT  
 CAAATTTTCTCCGTTTTCAGATGCATGATTGCATTTTAGAAAACCCCAT  
 CATTTGAGCCCCAAACTCCTTAAGCTGATAAGCAACTTCAGCAAAGTCT  
 CAGGATACAAAATCAATGTGCAAAAATCACAGGCATTCTATACCCAAT  
 AATAGACTAACAGAGAGCCAAATCATGAGTGAAGTCCCATTCACAATTGC  
 TACAAAGAGAATAAAATACCTGGGAATACAACCTTACAATGGACATGAAAG

FIG. 4 (15 of 61)

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ACCTTTTCAGGGTGAA...GCAAACCAC...CTCAAGGAAATAAGAGAGG...A  
ACAAACAAATGGAAAAACATTCCATGCTTATGGATAGGAAGAATCAATAT  
CGTGAAATGGCCATACTGCCCAAGTAATTTATAGATTCAATGCTATCCC  
CATCAAGCTACCATTGACTTTCTTACAGAATTAGAAAAAACTAATAGCC  
AAGACAATCCTAAGCAAAAAGAACAAAGCTGGAGGCATTGCTACCTGA  
CTTCAAACCTATACTACAAGGCTGCAGTAACCAAAACAGCATGGTACTGGT  
ACCAAAACAGATATATAGACCAAAAGAACAGAACAGAGGCCTCAGATATA  
ACACCACACATCTACAACCATCTGATCTTTGACAAACCTAACAAAAATAA  
GCAATGGGGAAAATAATTCCCTATTTAATAAATGATGTTGGGAAAACCTGG  
TTAGCCATATGCTGAAAACCTGAACTGGACCCCTTCCTTACAACCTTATAC  
AAAAATCAACTCAAGATGGATTAAAGATTTAAACATGGCTGGGCATGGTG  
GCTCACGCCTGTAATCCCAGCACTTTGGGAGGCCGAGATGGGTGGATCAT  
GAGGTGAGGAGATGGAGACCATCTGACTAACACAGTGAAACCCCTGTCTC  
TACTAAAAAATACAAAAAATTAGCTGGGCATGGTGGTGGGCGCCTGTAAT  
CCCAGCTACTTGGGAAGCTAAGGCAGGAGAATGGTGTGAACCCAGGAAGT  
GGAGGTTGCAGTGAGCCAAAGATCACGCCACTGCACTCTAGCCTGGGCAAC  
AGAGTGAGACTCCATCTCAATAAATAAATAAATATGGAACCTCTCCCAACA  
CAATAATAAGACAAACCCCCAAATGTTTTAAATGGGCAAAAATATTTGAA  
CAGACACTTCACAAAAGAGGATATGTAAATGGTCAAAAAGCACATGAAAA  
GATGTTCAACACCATTTGGTCATCAGGGCAAGAAAACCTAGAACCACAATG  
AGATGCCTCTGTACACCACTTAAATGTCCAAATTAAAGAAAAACAAGTTT  
GGCAAGTTGTGGAGCAACTGAAATGCTCGTGTATTGCTGGTAGAAAAAC  
AAAAATGGCATAAACCATCGCAGATAATTTGTTGTCAGTTTCTTACAAAGT  
AAACATATACTTTATTGATATGACAGTTCATTCCAAGAGAAATGAAAACA  
TAAGTCCACACAAAGACTTGTACCTGGGTGTTTCATGGTAGCTCTATTCT  
AATTGCCAAAATCTGGAAACAAATCAAATGTCCATCAGCAATGGAATGGA  
TATACAAATTGTGGTACACATGTACAATAGAAAACCTACTCTGCAATGGAG  
AGAAATTAACCATTTGACAAACACAAAAACATGGACAAACCTCAAAAACAT  
TATGCTGAGCAAAAGAAGCCAGACACAAAAGACTGCTCAGCGCATGATT  
CATTATATGAAATCACAGAAAGGGTCAGTTGAAGGTGCAGAGACAAAA  
GTAGATCTGCAGTTGCCTGGGGATGGGGTGGGAGGTTGACTGCTCTGACG  
CGTAAGGAAATTTGGGGGTAGGTGGGGGTGGTGGGAATATTTTTTTGAAT  
TGAATTTGGGTAAATAGTTTTAATAGGTAAAATATTGGACCCACAGTATT  
GAGATAGGTTTTAGTCAATTTAGACAGTTTATTTTGCCAAGGTTAAGGAT  
GCATCCGTGACCCAGCCTCAGGAGGTCCTGACAACCTGTGCTGAAGGCAG  
TCAACATACAGCTTGCTTTTATTCTCTTAGGGAGACATAATACATCAAT  
CAATGCATGTAAGGTTTACATTGGTTCAATCTGGAAGGTGAGGGAACTT  
GAAGCAGGGAGCTTCCAGGTTACAAGGTAGATTATTCTCAACAGAAAGGA  
ATGCTCTGGGTTATGATAAGCGGTTGTGGAGACCAAGGTTTTATCTTGTAG  
ATGAAGCCTCCGGGTAGCAAGCTTCAGAGGGAATAGATTGTCAAAGTTTC  
CTATCAGACATAAGGTCGTGTGTTGATGTTAATGCTGGTCAGCTTTTCTG  
AATTCCAAAAGGGAGAAAGGGTATACTGGGGCATGTCCAACCTTCCCTTCC  
ATCATGACCTGAACTAGTTTTTTTTCAGGTTAACTTTGGAATGCTCTTGGCC  
AAGAAGAGGGGTCCATTGAGATGGTTGGGGGGCTTAGAATTTTATTTT  
GGTTTACAGTGAAGACTTTTCAAGCTAGACACTTAAATGAGTATGTTGCA  
AAATGGCAATTTCTTAGCACGGC

>Contig39

GACGTCCTAAAGAAATGCTAAGGTAACCTCAATTAACCTATGCTAGAAAAGA  
GAGTTAAGTATTTAGGAGGATTTAATATGGTGTAAAGTTGTGAAATCA  
AAATGGAGACACTAATGTTAAGAAAACCTGATAAATGGAGCCAGGGAAG  
GCCATGAAGAAAGAGTTCTCACTTGTATCCCTGATCATGAAAAAGACT  
CTGCAAAAAACAAAACCTTGACAAAGGCCATTGCAACCTTACACAAAA  
ATACTACTTTAAAGGACATGTGCCAGCAACTGCCTGTCCAACCTCAGA  
CTGGCAATATCTTTGTTATTGATCTTAGTAGCCAGCATAACTATTTCAA  
AACAGTGATGTAATGCTCATTTTTTTTCTTTTGAAAACCTTTGTCTTCT  
GTAAAAACCTTTGTCTTCTTACTTACCCTGAATATGCACAGAGTTTACT  
ATGGAGTGCAATTCCTGTTGCAATGCTCTATTCCCAACAAACATCATT  
TTCTTTTAGAGAGCCTCTCTCTGTTTGTGATTTAGGTTGGTGATGTAAAG  
CAATGGCATAACTGAACACTGATTCAAAGAAAAGTGGCTTTTCTCTTTGT  
TGATTAAAAAGAGGCCTTATAAATAGGATAGTAAGATTTGTAAGTTGAA

FIG. 4 (16 of 61)

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CTTAAAGCATGAAGAAAATTTAGGGGCCAGGCAGGGTGGCTCACACCTGT  
AATCCAGCACTTTGGGAGGCCAAGACAGGAGGATTGCTTGAGCCAGGA  
GTTCAAGACCAGTCTGGTCAACACAGACCTCATCTTTACTAAAAATAAAA  
AAATTAGGCCAGGTGCAGTGGCTCATGCCTGTAATCCAGCACTTTGGGA  
GGCCAAGGCGGGAGGATCACTTGAGGTGAGGAGTTCGTGACCAGCCTGGT  
CAACACGATGAAACCCCATCTCTACTAAAAATACAAAAAATTAGCTGGG  
TGTGGTGGCGGGCACCTGCAATCCAGCTACTCGGGAGGCTTCAGGCAGG  
GGAATCACTTGAACCTGGGAGGCGGACATTGCAGTGAGCTGAGATAGTCC  
CACTGCACTCCAGCCTGGGCGACTCAGCAAGACTCTGCCTCAAAAAAAA  
AAAAAAATTAGTCAGGTGTGGTAGCACACAGCTGTGGTCCAGCTACTC  
GGGAGGCTGAGGTGGGAGGATCATCTGAGCCAGGAGGTCAAGGCTGCGG  
TAAGAGCTGAGATTGTACTACTGCATTCCAGCAGGGGCTACAAAGTGAGA  
CCCTGTCTCAAAAAAGAAAAAGAAAAAGAAATTATGTTTTTAAATTTA  
TAATTATAATAAATTTAATTACATAAATTTAAGCTCAAGTAATTGTAAAT  
ATTCTTTCTGTGCACATAAGTTATTCTTGATTGACCCACAGGAGCTGG  
CCATTCTTCAAGTCAGAAGGCCTGAGAGAGGAGCTGCCAGGTGGTCTTC  
ATGGGGCTGTGCGGCCAGTCATCCCCACAGGTTGACAATCCTTGTTGAC  
TTCATCCTCGTTGGATCCTCTGTATCCCTGACGATGAGCAACTGTGAGGC  
CCGTTTCAGCACTGAGTTCCAGTCAGGAAAAATCCACCCACCCACCACA  
CGCTCACACTTACACACACATTACACATGCACACACGTTCTGGCTCCGA  
AAAAGAAAAAAGCAATTTAAATAATTCTGATCCTTTGCTTATTT  
CCACAACTCCATGAAAATTGTACATTGTCCAAGCAACATTTCTTAATAT  
TCTCTTTTCTCTCATATCCATTTTCTTACTGCTGTCTCCACCTTTCTC  
TTCCAACTCCCTGTTAAATCCCTGCCCGAGCGAATTTTATTCAATTT  
TGTGGAATGGAGGCTGCTCTGATTAAATTAAAAAATAAATTTTCC  
TACTCCATGTCCAGATCCCTAGTTGTTTTTGTGTTTTTGTGTTTTCTGAG  
ACAGGGTCTTGTGTCTTCCATGCTGGAGTGCAGTGGCATGATCATGGCTC  
ACTGCAGCCTCAACCTCCTGGGCTCAAGTAAATCTCTTGCGTCAGCCCTC  
CCCAGTAGCTGGGAGTTCAGGTATGTGCTACCATGCCTAGCTAATTTTTT  
TCTTTTATTTTGTAGAGACCGGTCTTGCCAGGTGGCCAGGCTGGTATA  
GAACCCCTGGGCTTAAAGTGATCCTCCTGCCTCGGCTTCCAAAGTGCTGG  
GATTACAAGTGTGAGGCACTGCACCCAGGCTGGATCCCTGCATTTTACA  
GATTTAGCATCACAAAGTCTAAACAATTAGACTGACTAAGGCAGAACTG  
CCCTTATGACAGCAGACATAAGAAGGAAAAGGCCAAAACACTGTGTTAAA  
AATTATCCAAATGTGAGGAAAAGGCCAAAGAGAGTAGGTGTGCCTTTTAG  
TGTCTAAGCTGCCTGCCAAGGGGCATCTGATGCTCTCAGGCAGGAGTCC  
ACAAATTTTTTTTGTAAAAGATCAGATAGTAAATCTTTTCAGCGTGAAG  
AGCATGAGTCTCTGTCAAAATACTCAACCACCATTAACAATGAAAGC  
AGCCAACGACAACACATGACAAATGAGTGTGGCTGTGTTCCAGTAAATC  
TTGATTACAAAAACAGGCAAGAGGCCAGAGCTGACCCATGGGCCATAGTT  
TGCTGACCCCTTCTGTAAAGGAAAGTATTTTGTGTTGACTTGCTGTTTAC  
CATTGATTGAACACAAGGCTCTGTAGAGTTACTTGTTAACTGCAGAAGA  
TTGATGAGTGGCAAGTAATTTTATTACCAGAAATATANNATTATTCTGT  
TCAGTAGATAAGATAAACCCACTGTTATATTACTGTCTTGTTTAGAATGT  
GACTTTGATTCAATTTTTTCAAAATTCATATTATTGCCCTAATTTGTATA  
TAAGTATGCTTCTTTTAAAAATATATATTTTAAATAAATTTGAGACAGG  
GTCTCACTAGGTTGCCAGCCTTTTGCTATAATGAGAGCATAAAGTGAAT  
TTCACACTTTAGCCTAGTGCATAGATGGGATTACAGGCACAAACCACTGC  
ATGCAGCTAACTTTGCTTCTCATTCCAGCACGTTCTATTCCNNNGNTTTT  
CATATACGCGTCTCTTAATGC

>Contig40

CGCATTGAGCCCAAGTTTTCTTCAGTGTTAAGGTTTTTGTACTCTGTGC  
CCAAATGTCTTCCAAAAAGGTTAAGTTTTTTACCTTCTGCCAACATT  
ATATGAAAGTGTCCACTTTTGTAGACTTTTACCAATGCTGACTACTTTT  
GTTTCAAAAAAGCTCTCAGTAATTTTCTATTAATTACTTTTACCCTTTT  
TATTGAGGGTGTTCAACTTTTTATTGTTAGCATATTCTCTGCGCTCCA  
TTGGACGCTTGGCAGCTTTTTGGTAGTAGGTGCCTTAGAAAAGTCCTT  
CTCGTCTGGCCCTTCTGAGCAAATCTAGTGAACAGAATTGGCTCCATGC  
TCAGCATTGCTTAATACGGTTGATCCAGGGCCTAGGACTCATTCTTCAT  
TACCATCCACTTGCATTGTCTTAAAGCAAGGCTCTATTAATTTAATTTGG

FIG. 4 (17 of 61)

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CATTTCCGTGTCCTCAGCTCTTAGTTCATTAAACAAAGGCTTTAGAAAAC  
TCCAGTAGATGCCTATGTTGCTTCCTTTTAAAAAATTTTGGAGCTGTTT  
CCCTAGCCTAACCTTTTCTTCAGGGCAGGAGTTAAGTCCCTTCTACTGCA  
TTCCCTGTGAAGATGGTGATTCAAGAGGCAGGGCACCTGTTGCTTTGTGAA  
ACAGTCCACTCTGCAGCTGGGCAGCTCTGTTACTAGAATGTTCTCCCTTC  
TGGGGAGCCAAATATTTTGATGTCTCTGTGAATCTCATCTGCTTATCCCA  
TCGTGTTTATGTCCTTGAAGATGCACAGGTCTGACACCACGAGGTAGCCCT  
TAGAAAATTTGATGGCATTCTGATGTGTCCCAACTCTTCTCCAACCACT  
CCTCCCAGAGCTTGTTTCTTAAGCCCCCTTGTGGAGCTGATTGCTTTCCTC  
AAGGCAGCTCAGTTTTTCCCAGTTTGCTCCTGGTGGTCTGAAATATGAT  
TGACTCCTGAATACTCCAGGTGTGAAGGAGAGTGGGGTGGCCTTTCTAC  
TTGTCTATGGCCTGGGTTTTAAGTTGCTGTCCAGTGGAGCAGAGGTGACTT  
TCCCAGTGAATACTATTTTTTCCCCTCTAAATCCTTAGCAATTTTGTCTC  
CAGAGGCAAGACCTGGCCAAACCATTTGTGTTGAGGATTGAATCAAGAAT  
GATTGAGGAGATGACAGTAGTCCCCCTCATCTGAGGAGGGCGTGTCCA  
AGCCCCCTCAGTGAATGCCTGAAACTGTGGATAGTACCCAACCTTATATGT  
CTATGATTTTCTATAAATTAATACATGCCTGTGACAATGTTTAAATTTAT  
AAATTAGGCAAAGAGGGCCAGGCGCAGTGGCTCAAGCCTGTAATCCCAGCA  
CTTTAGGAGGCTGAGGGCTCACCTGAGGTGAGGAGTTCGAGACCAGCCTG  
ACCAACATGGAGAAACCCCGCCTCTACTAAAAATACAAAATTAGCTGGGC  
ATGGTGGCAGGCGCCTGTAATCCCAGCTACTCGGGAGGCTGAGGCAGGAG  
AATCACTTGAACCCGGGAGGCGGGATTTGCGGTGAGCTGAGATCGTCTCA  
TTGCACTACAGCCTGGGCAACAAGAGTGAAACTCCGACTCAAAAAAAAAA  
AAAAAAAAATTAGGCAAAGAAAGAAATTAACAACAATAAGTAATGAAATAGA  
ACAATTCTAACAATATACTATAATAAAAGTTGTATGAATGTGGTCTCTTT  
CTCAAAATTACCTTTTTTTTTTTTGGAGACAGGGTCTCACTTTATTGCCCAGG  
CTGGAGTGCAGTGGCAGCATCACAGCTTACTGCTGCCTCGACCTCCTGGG  
ACCAAGTGATCCTCCCACTTTAGCCTCCTGAGTAGCTGGGACCACAGGCA  
TGCACCACTGTATCTGGATAAATTTTGTATTTTGTGAGAGAGAGG  
AGGTCTCACTATGTTTCCCAGGCTGGTTTTGAATGCCTGGGCCCAAGGGA  
TCCTCCTGCCTTGGCCTCCCAAAGTATTGGGATTACAAGCTGAGCCACC  
ATGCCTGCCCCAAATATCTTATTGTTCTATACCACTCTTCTTCTGT  
GATGATGTGAGGTGATCCATTGCCTCCTTGATGAGATGAAGTGAGGTGAC  
TGATGTGGGCATAGTGATGCAGTGTTTAGGCTGATATTGGCCTGATGATA  
TGTCAGAAGGAGGGTCATCTGCTTCGGTGATCCTGGATCATAGAGTCATG  
ATGATGTCAATGGTTGGATGTGAGGAGCAGACGATGTCAATGACTAACGA  
TAAGCTGGACAGGTGGGATGGTGGCACAAGATTTTATCACGCTACTCAGA  
ATGGAGCACAATTTAAACTTCTGAATTGTTTATTTTGGAAATTTTTCAT  
TAATATTTTGGATTGCAGTTGACTGTGGGTAACTGAAACTGTGGAATGT  
GAGACTGTGGAAGAGTGAGGGAGTACTGTATTATGGAACGTGAACCTCTAT  
TCGGTAGGGGAACAGAATTCACATTTGTGGGGCCAGGTCTCTGCATCTG  
TAGGGATCCAATTGTTTCATTTCTCGTTGTAGCAAAACTTGGCTTTGGA  
ATCAGACAGATTGATGTTTGCTATCATTCTAAATGGGTGCAGCTACACTT  
TCCTCAAGAGGTAGTTCTGAAAATTTAACAATAATGTGAATTTCTGGTAA  
AAAAAAAAAACCTCAAAATATTAGTTTTCTTTCTTTGTGTCTGATGT  
ACTCCATCAAATACTGGGAAATATGTGTCTCTCATAGAAATGTCATGGAT  
CTTTGTAATTCTGATTATCCACAAACCTTGGGGATTAGCTGTTTCAATGT  
TCCTATTTTACAGATAAGAAAATGGAGCCTGTGGTAAGTTAAGTGAGTTA  
CTCATGGCTACTTAACTAATATTTTACTAGGTGATAGGCCAGAGCTAGAG  
CCCAGGTACCTTCTTATCAATGCTCTGCCTGTCTCTGTGCTTCTGT  
CTGTCTGTATGTGTATGTGCCTGTTGACAGTAAGGCATAGTTTAAACCCAG  
TAGAACTACCGGTTGTGAATGAATTCACCTGTGAAATGACTGACCATTCA  
AGGAACAAGTGTTTTTCTATGCTTGACACCTGTTTTGGATGCCAAAAG  
GATACAAATGTAACCTCAGACACTCTGGGCCTCATTTTGCACCTATTAGC  
ATGTCCAAAATTAAGAAAGACTGACCACACCAAATATTGGTGAGGATGTGG  
AAGAACGGGAACCTTTCATACACTGCTGGTGGGGATGTAAATGGTACAAT  
CCCTTTGGGTAAACAGTTTGACAGTTTCTTAAAAAGTTAGACATATATATT  
TACCATATGACTCAGCCCTTCCACTTCTAGGTCTTTACCCAAGAGAAATG  
AAATGCTGTGCTTTTACAAATGTCTATACAGGAATGTACATAGCAACCTT  
ATTTGTCAATTGCAAAAAACAGAGACAATTCAACGTTGTCAAGAGTGAATG

FIG. 4 (18 of 61)

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GATGAGCAAGCTGTGGT CTCTATGCA...GGTATCCTACTCAGCCAG  
AAAGATATGGCTAAT  
>Cont:1941  
GACAACAATGTCATGCATAAGATGACGATGGCCTGGGTGATTGATGCAAA  
CAAGGATAAAGAAAAATAATCAATTTTGTCCCCATTTTCAAAGACAGATAG  
CAGCAGCAAGAGTGTAAGTCTGAGGAAAGTCATATTCCTTCCTCCTACAA  
CATAGCACACACACTTACAAAAACAATACACAGACTCCTGGCCAATGGAC  
TTCAAAACCTGAGGAGGATCATTAAATTTAAATGTTCCACCGCTGCATGAAA  
TCTCCCTGGGTCTTGCCCTCCCTTCCCCACCCTCCTCCACTTGGGCCGGG  
GCACAGCAGTGATTCTCTCACCTCTCAGAGTGAGCCAGTGTTGGCTGCAT  
TGAAGGCTCCAGATATGCAAAACAGGGCAGATATTCCTGGACCAGGGTGCA  
CAGAGTGAGGCTCCAACGCACCCTATTAAGTGCATGAAGGATGAATGAGC  
CTCTGGTATGGGCTGGGACAGAAAAAGGATTCAAGGGGCCCAAAAGGGT  
TTGGGTGGAACCTACCAGGAGCGGCAGTACAGACTCCTTGGGAAGGTGGC  
CATGATTTAGCCACATTACCAATAGGATAATCTGGAGAATTTCTAGCT  
TGAGTTTCTGGGAGAAAAGCAGATTTCTGGATTATCTGGTGACAGGTAACA  
GGGCCGAGTTTCATCCACAGCCACCTGCAGTGTTAGCACCTTAAGCTGAGT  
TCCTTGCCACCAGGATGCTGTACGCCCAGTCAGTGAGACGGTTCTTGG  
CTGAAGGACTGAAAAGCTTGGGTAAGTGACTTCACCTAAGCCTCTATCTC  
TTGCTCCCGTAAGTCAGGGCTCATTGTGGCTCCTTGCCAGGCTTGACTTCA  
GGGTTAACAGAGAAAATGAAGGTACAAGTGCCTTGTGAACCTCTGAAACTC  
CAAACAGTCATTCTCAAAGTGCCGTCCACCAGTCTAGCACATCAGCATC  
ACTGGAAGCTTGTGTTGAAATGTAAATTATCAGGTCCTCCAGAGCTATGTA  
TGAATTAGAACTCTGGGAATGGGGCCCTGCAATCTATTTCAACAGGTCC  
TCCAGGTGATTCTGATGCAAGTTAAAGCCTGAGAACTCTGTCTATACA  
AATGGATGTCAACTCAAGCTGCTCTTCAGAATCACCTATAGCACTTGTTT  
ACCCGAATCCCTGAGAATGGAGCTTCAGGACTGCTATTTCTCAAAGTTTG  
CCTGGTGATCCTGAGATGGGGTTTGGGGGACAGAGATCCAAGGTGCTACC  
AGGTGTGAGGAATTGTTAGAAGGCAAACCTGGCTGTCTAGGGTGCTT  
AAAGGGTACAGATCCTAGGATTCTGCCTCTTACAGCTGAATCAGACTTTC  
CTAGAATGGGATTGCTGTCCAATGGCATGCCTCCTGGGTGACTCTGATGT  
ATAGCCTGGGCTGGGAACCACAGAGGATTATCTTCCATTGACCAAGCTG  
ACAAACTCGCTTAAGGCTCTGAGTTTCACACTTGATTTTCTAGCCCCTGT  
CCTTCCATGGATCACCTGCCCCCTTCCCTCCTAATCAGGAGCACAGTCAG  
TGGATGCACCTAATGTGGCCTCTCCTTGGCTGCAGGGAACAGGTGGAAATG  
TGGCCATAGGTGTGCAGGGCTGCCTGCCATGTATTAATAGCTACAGATT  
GAAAGATCCAAGGACAAGAGACTAGAAAAAAATTTAAAAACAGCCAAGCAT  
TGGCCCAGTAATGGCATTTCAGAAATCCACCAAAATATTAAGATGCTTTT  
TGAAAAATATCCAGAGCACTCATGTAAAAGTGCTTAATTATTAATAAAAG  
CTGACATGTGTTGGGTACTTCTGTGGGTCTGGCACTAGGCTAATTATGT  
TTTTAGGAGTTGACTCAAATGCTCCCTGTCATAATTATGTGAAAAAATAT  
AATTATTAGCTCCATGGTACAAATTAAGGAGAGGTTACATAAATAAAAAG  
GAATGATACTCAAATTAGTAACCAAGAGCCCATGCTCTTAAACACTATGCT  
ATTATTTGTGACTCTTACATAGGTGGCAAAAGTCAAAGGCTAGATTGAC  
TTCTGTCCACTTCCAGCCAAGATGAAGTACAAGATTCAGATACACCCTTC  
CGCATTAAACAACCTTAGGAATCAGACAAAATATACAAAGCATTGTTTGT  
ACACATTGGATAACAGACAGCACTAGATAGTCGTGTCTGAGAAAAGCGGT  
GAAATGAGCTGAGTCTTAGAATTGCCCCAGTTTACTAAGGGGCATAGTAA  
GGGCATAGCTGCAGCACAAAGAAGCAGAACCCACAGAGACTGGCGTTCA  
CCTGAGTTGAGAAAACCAAGTTGAAAATTTAGGAACACTAACACAGATAT  
GTAGGCAAGAGTATCAGAGAGGAGACAGTTGTAGGGAAAAAGAGAGCTTT  
ACAGAGAGACAGCGAGAGCTCCAGAGACCCGAGAAGATTGCCCTGACGT  
CACTAGCTGAGTACCGATCAGTGCATACATGTAAGGATATTACTCAATAT  
GTGGAAAAGAACAGAAGGAATGATGTCCAAAGCTCACCCAAAGACAGGAA  
TCATTTATGTTTCCACCAGCCAGAGTGGAACAACCTTGTAACGCATATGG  
AGTACTCAAACGAATATTTCTCAATAATAAGTTCAAATTAAGTGAAGT  
AAAGCCTGCCCGCTTTGTCTGGACATGCCTAACAAAGCTTTGAGGGAAGC  
CTCAAAGAATGAAACCGTGTCCAAGTAATTTAACTGTGTCCAGAAAAA  
AATTCAAGAACATTTAAATAAATATTAATAATATGATCAAAACCAGCAAGG  
TTAAATTCAAATGTCTGGCATCCATTAAAAAATTACCAGCCTTGAAAAAT

FIG. 4 (19 of 61)

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TGGCGGGAAAAATATTA: .ATAATGAA. .JAAAAAGCAATCAACAGAN  
AGGCCTAGAAAGTATACATATGATAAAATTAGCAGACATTAAATGGTTAT  
GATTAATTTATTTTATATGTTAAAGAAGGTAGAGAAGAGCATAAGCACAT  
TAAAGAGAGACAGGAAAGTCCAGTACTCACACAGGGCCAGGAGCAGTTT  
TCACCAGTCAGGTGGGAAAACCTTCATATTTTCATGGAGCATTGGTAGAGTA  
CACAGTGTCTTGCCTTAGTAGAGGGATAAATGCTGTTCTGTTCCCGCCTA  
ACCCATCTTGAAAGAAAATCTGAAAGGATCAAACCTGTATTCAAGTAACCT  
AATCACATCCAGCACACAGCTCGACTAGTTATAAAAAACAAAAATATTA  
ATATCTAGAAACACAAAAATAATATCTAGCACCCAACAAGGTAAAATTCA  
CAATGTCTTAGCATTCAATTGAAATTTTCTAGGCCATCAAAGAAGCAGTAA  
AATATGACCTATAAGGCCGGGCACATTGGCTCATGCCTGTAATCCAGCA  
CTCTGGGAGGCCAAGGTGGGTGGCTCACCCGGAGGTCAGGAGTTCAAGAC  
CAGCCTGGTCAACATGGTGAGACCTCATCTCTACTAAAAATATAAAAAAT  
AGCCCAGCATGGTGGTGGGCGCCTGTAATCCAGCTACTCAGGAGGTTGA  
GGCAGGAGAATCGCTTGAACCTGGGAGAAGGAGACCGCAGTGAGCCAAGA  
TGGCACCATGCACTGCAGCCTCATTAGAGAACATCGGGAAG  
>Contig42  
GAAACTAAAGGCTTATTTAAAGCGCGAGACCGTGGCGCCTTTGGACTGGA  
CCCTTTCTAATGATCATTAGTATCAGGCTATGTGGGAGTTGACCGTTTT  
GCATAGCCTGAAAGCCAACAGTATCACTCCTCCTTAGGTGTGGCAGAGA  
TGTGAGAGAAGGAGACTGACAGTCTGTGGGTGTGTATGCAGTGTGGGG  
AAGCGAGGCACAGGGGACAATACTGTGGTGTAGAAAACCTAGTCTAAGGTA  
GCATCAGGAAATTCATGAAACCAAAATGAATTCATAACAGCACAAGACA  
TTATTTGTTTTTGCCTCCCTCTCATTTTTTTTTTTTTTTTGAACAGAGTC  
TTGCTCTGTATCCATGCTCGTGTGCAGTGGTGCAATCTCGGCTCACTGC  
AACCTCCACCTCCAGGGTTCAAGCAATTCTCATGCCTCAGCCTCCTGAGT  
AGCTGATTACAGGTCTGCACCACCCCGCCGCTAGTTTTTGTATTTTAG  
TAGAGATGGGGTTTTGTAAATGTTGGCCAGGCTGCCCTGTCATTTTTTTT  
TACTAGTGTCCAGTGGAGTTTTTAGGGGTACATAACATGATACTGTCA  
TTAATCTAATGGCTAATGAAAGGGATATGTATATGTTTTTGTGTTTAAAA  
CAAACCTCTTTGGGGTCTCAATAATTTTAAGAGTATAAAGGGTCTTG  
AGATCAAAGAGTTTGAGTTCTGCTGGACTGGGACAGTGGTTGTCAACCCA  
GATTGTACATTAGGGTCATCTGGGAAGCTTTAAAATAGTACTGATGCCCA  
ACCTTACCGCAAACCAATTAAGCCAGAATCTCTGTGGATGAGAAGTCTTC  
ATTGTCATCATCACCATGACCATCATCATTGTCAACGTCCTACACCATT  
ATCATCATCATCATATCATCTTCATTATCATTGTTAGTATCTCCATCACC  
ATCATCAGCATCACCATTATTATCATCATCATCATCCCCACCATCATCCT  
CATCGGAACCTCACCTGCATGGAGGACAATCCACTATGCATTAGGTGCTA  
TGCTATTTGCTATACTCCTTATTCTCAAACTGCCAGAGAGGCTGATAT  
TATCTCACTTTATAACAGGAGGAATCTGGATCGGAAAAGTTAAGGTAAGC  
TAATTCACAGAGCGAGAAGAGATAGAGCCAGGATTGAAACAGTTCTCT  
GCTACATCAATGTTCCAGTCTTGCATATTGAGAACCTCTTTAGTTAT  
GCTTTCACCCCTCCAACACCACAGTAAATTTTTCTTTTTTAAAAAAT  
TATACTTTAAGTTATAGGGTATATGTGCATAATGTGCAGGTTTGTACAT  
ATGTATACATGTGCCATGTTGGTGTGCTGCACTCATTAACTCGTCATTTA  
CATTAGGTATATCTTCTAATGCTATCCCTCCCGCTCTCCCCACCCCATG  
ACAGGCCCTGGTGTGTGATGTTCCCCACCCTGTGTCCAAGTGTCTCAT  
GTTCACTTCCCACCTATGAGTGAGAACATGTGGTGTGTTGGTTTTCTGTCC  
TTGTGATAGTTTGCTCAGAATGATGGTTTCCAGCTTCATCCACGTCCCTA  
CAAAGGATATGAACTCATCCTTTTTATGGCTGCATAGTATCCATGGTG  
TATGTGTGCCACATTTTCTTAATCCAGTCTATCATTGCTGGACATTTGGG  
TTGGTTCCAAGTCTTTGCTATTGTGAATAGTGCCACAGTGAACATTCATG  
TGCATGTGTCTTTATAGCAGCATGATTTATAATCCTTTGGGTATATACCC  
AGTAATGGGATGGCTGGGTCAAATGGTATTTCTAGTCTAGATCCTTGAG  
GAATTGCCACACTGTCTACCACAATGGTTGAATTAGTTTATAGCCCCACC  
AACAGTGTAAAAAGCATTCCTATTTCTCCACATCCTCTCCAGCACCTGTTG  
TTTCGTGACTTTTTAGTGATTGCCATTCTAACTGGCACCACAGTAAATTT  
TTATAGATTTTATAAGCAAATTTGATTTTACTGTGCAAGAATTGGTTTATT  
TTTTAAACCATGTGTTGCAAACATAAATGGTTAATTGTGATATTTGCTC  
AGTACAAGATCATCAGATCACTACACAGACTTGAGGTAATTCACCTAAA

FIG. 4 (20 of 61)

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AGCAAAGAGAACTGACCCACATTAAGTGAAGAGTCTTTACTTATTTA  
CCCTATAAACGAGCCAATATGAAGAGAAGGCCTTAATGTGGTTAACTATG  
TAATTTTTTTCTGACTTTTTGAAATACTGAGAAGAGCTCATGACTCTCCC  
ATCTCCTAATTCTACCTTGGTGGATTTTAGACTGACCACAACCTCATGGGT  
AAATGAGGGAAGACGAATAAGAAACCTTGCTTTTTTTTCTCCTTGTTTT  
TGGCTGGCTGCAGTGGCTCACACCTGTAATCTCATCACTTTGGGAGGCCA  
AGGTGGGAAGATCACTTGAGCTCAGGATTTCAAACCTGGCCTGGGCAACA  
TAGTGAGACCCCATCTCTAAAAAAGGCGACGG  
GCGGTGCGTGCTGTAATCCTACCTACTCAAAAAGCCGAGGTGGAAAGAT  
CACTTGAGCATGGGAGGTCAAAGCTGCAGTGAACCTTGATTGCACCACTT  
CATTCAGCCTGGGTGACAAAGCAGGACGCTGCCTCAAAAAACAAAAAC  
AAAACCTTAATTTTTTGGCTATTCTTTCTGGTAAGAATGGTATAGAGAT  
GGGATGAGGATGGCTATTGTATGAGAGAGCAAACAGGGTCCAAGCAGTG  
CTCTGGGCTGTCTAAGGACCAGTAGTCAGCTTAACCTTCTCAAATTTCCAG  
GGAAGGAGTTCGGAGTGGTAGAATATCCTGGGTATGCCAAAGCATCACC  
TTGCAATAGCCTGTCTGAATAATTTGTTTCATTTGTTATGACTGGAAA  
CTGGCTTTGTGTATGCCAGAGAATGGGGGCAGGAAAGAGAGATTGGTGTC  
TTGAGCTCTCTGTGCCTCTGGGGCAGTGATGCTTTTCTCTCATGTGGAA  
GGAGAGCATGACTGAAAAGGTGCACAAATAAGGTGTCTGTGAGAGAAAT  
AACCTTCAGATACAGAGACACAACCTTCCCCAAGAGGTCTCTATTGCTC  
TGCTTTTTTCTTTTTTGGCTTGTCTACCATTAATAACAGAACTGA  
TTATGACCTCAAAGAGAGGAGAAAGCGACTCTCCCAACCTAGAGCTAG  
TTAACCACCATATCTTCTAGATCTCAGTTCAAGAGTCACTTCCATCCCC  
AATAAAGCCCTTGAGTGCTGAGCACCTCTCCGTATAGCATTTGTCTTA  
GGGGTTTTGTACATTTCTTGTGTGAAACTTGGGTTGACATCTGTATTT  
CCGACTAGATTACAGTTTCTCAAGGTAGGGATGTCTTGTCTGCCATTT  
TCAGTTCCAGCATCTAGACAGTACCTCAAGCAAACAAGGCCGAGGGGGT  
GCGGATCACGAGGTGAGGAGTTGAGACCAGCCTGATGAACATGGTGAAA  
CCCCGTCTCTACTAAAAATATAAAATTAGCCAGGCGTGGTGGCAGGTGC  
CTGTAATTCAGCTACTCAGGAGTCTGAGGTAGGAGAATCGCTTGAACCC  
GGGAGGTGGAGGTTGCAGTGACCTGAGATCCACTGCACTCCAGCTTGGGT  
GACAGAGCAAGACTTCGTCTCAAAAAAAGAAAGAGAGAAA  
AGAACATCAATGAATGAATGAGTGAGATGAATGAGTTAGCAGTGTTGGA  
TTTAAGTGTCAGATTCTTCCAGCTTGACTTTTTCTTTGGCTTAGTGAT  
TTTGAGGTCNCAAGATTTATTTTCTTTTCAAAAGGTGATCACTACCATA  
AGATCTTCAGAAAAGAAATGTGGCAAGCCANGTCTCACTAATGCAATCT  
CTATAACAACCTGTATCAGTACT

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GAGGTGTCATAAATATGGACCGATAGATGAATACAGGTAGGATGGGACAC  
AATCTAAGATCCCAGGGGGGGGAGACCACACGCTTGGTTAGGGAGACCCA  
AAGTGGACCGTGTGGCCAGAAGAGTCCCGCACTGCACTCTAGTGACAGTG  
CAGAAAGTCACTGTGGGAAATCTAGAAGTTTCTACAGGTTGCTATTTCT  
CATAGCACTGTGCAGGCCAACCTTCTGCTCCACTGGCTGTGGGAAAA  
GCTTTCTCTTTTCTTCTAGCCAGGGAGCTCTCAAAGTGTTCACCTCTCT  
CACCTCCACCCAGGCGTCCAGGTGTGGAGGACACTGCCGCTGCTTGTCT  
TGCTGACTCATCCCTTGGTTTTCACTTGGAAAACCTACCACAGCTGGCCT  
CTTTCCAAGCATCAGCCTCCTCATTTTCTTAATCCCTTAGGTGTGATCTC  
ACCTCCACACAGTAGATTGCCTCAAGGCCCAATTCCAATATGAATAAAAA  
TGATTATTTGTATCTTCCAATCTTCTTTTAAAAATATTATTTTATAAT  
TCCCTTTAGGAGGATCACCTAAGTGAAGACTATTTTACCTAAGAAATGT  
TAAAATGTAAAGACATGGTTGTAATCTGGGGATTCTGTGTTAAATGGCTA  
GCAGACAGAAGTCAGACGACAGGCTAGAAATGTGTGAAGAGTGGTTGCCT  
TTGAAAGGCGGAGTTGGTAATGATTTTCTTCCATTTTCCATGCTTTCCA  
ATTCTCTACAAAGGCCTTAATATTACTTCGATAACCAGGACCTCTGATAA  
CCTGCCCCCACCAGTAAAGACTTAGCTGGGAAAGTCAGCTTCATGTGAG  
GTAAAAGGAACCAGGTAATACACAATTCCCACTGCCAACTGTCCGGGTGTG  
CAGGCCTGAGCTTCTGTCATGTGGGAGGAAAGAGAAAGAGAGAGAACT  
CCAAGATCCAAGATCCAGCAAGAAGGCTGGAGTCTGAGGACGCAGAAA  
GCTGAATGGCACAGTTACCACTATTGTGCTGAGGTTCTGTGGCCTCTGGG  
TCTCTTGACAACCTGGGCAAAGACCCACAGAAAACCTATCTCTAGACCCTAC

FIG. 4 (21 of 61)

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CTGTGGGAGGGGAAAGTCTTCAGATCACTACAGGACAGCCACCTGGAA  
CTCAAATGGCTTACAGTTCTTTCATCCAGAGGGTCTTTCATCTAGTACATA  
CCAGGTGCTAAGCCTGGGTGCTGGAGACATGACGGGGAACCCATTTACCA  
TGGCTTTGTTACTGTGACATTACATCTAGGGAAAGCCAGCAAAGGGGAG  
GGATCGAGGAGAGCTTGTAGGCAGAGAAAATACCCAAGGGCAAGGGAGA  
AGCCAGCCTGTTCTGAGCACACACAGTGGTTCATCTAACTGGGCCTCAG  
TGCCAGGTTGGAGATGGGGCTGAGGAGCTGTACAGAGCATTCTG  
GACACAGATGTACATAGTCCCTTGAGGTTAGGGTCTTAGGCATGGCAG  
CATTGCTTTGAGTTTTCTTTTGTAAATGTTGCCATTCATGACAATGTGG  
AAGATGGGTCTTTCAGAGAAGGGCAGGGCTGTGAGACCAGTTAGGAGAC  
TAAGATGTGAGCCAAGGAAAATGAGGAACACCTGAACACTGGGGCAGGTG  
CAGGGCCCAGAGAGAAGCAGATGGCTTCTGAGGTTTTAAGTAGGTAGAA  
TCAAGGCAGTGGTAAAGATCTTTATTACATATAAACTGGAAATAAGCCA  
TCTGCTCCAAGACAAAAGAGTAGGCGGAAAACAATACAAGACAGAAATGG  
AATTAGAACAAACCTGGGAGGAATGTGGAATTAGAGTAGAGAGTCCAACA  
CTGGCTGCAATCATAAAAAATGTAACAAACAAAAATTTGCTAGGTGTGC  
TTACTTAGAAATAATTAGCTGTCTATTAAGTTCACTTGTGTTATGGCTT  
AAATGTGTCCCCAAAATGTGATGTGTTGGAACTTGATCCCCAATGCAA  
CAGAGTTGAGAGATGGGACCTTTAAAGGTGATTAGGTATAAGGGTTCT  
GCCCTCATAAATGAATTAATACTGTTATCATGAGAGTAGATTCTTGATAA  
AAGGATGATCTCTGCCTCTCCCCACAGCCCTCTTGTGCATGCTTCTCTG  
CCTTTCCACCTTCTGCTATGGGATGACACAGCAAGAAGGCCCTCACCAGA  
TGCAGCTCCTTGATCTTGACTTTCCAGCCTCCAGAAGTGAAGCCAAAC  
AAATTTCTGTTTATTATAAATTACCCAGTCTCAGGTATTCTGTTCTAGAA  
GCACAAAATGGACTAAGATCATTAGATTATCATTTTTATCAGACTGTTG  
AAGTGAAAAATAAAATCAAATAAAGAAATTAAGAGAGCTGCATGCAGCA  
GCTCATGCCTATAATCCCAGCACTTTGGGAGGCCAAGGCAGGTGGATTGC  
CTGAGCTCAGGAGTTTCAGACCAGCCTGGGCAACACGGTGAAACCTGTT  
TCTACTAAAATACAAAAAACTAGGCCGGGCGCGGTGGCTCACGTCTGTAA  
TCCCAGCACTTTGGGAGGCCGAGGCGGGTGGATCATGAGGTGAGGATC  
GAGACCATCCTGGCTAACAAGGTGAAACCCGCTCTCTACTAAAAATACAA  
AAAAAATTAGCCGGGCGCGGTGGCGGGCGCCTGTAGTCCCAGCTACTCGG  
GAGGCTGAGGCAGGAGAATGGCGTGAAACCCGGGAAGCGGAGCTTGCACT  
GAGCCGAGATTGCGCCACTGCAGTCCGCAGTCCCGCCTGGGCGACAGAGC  
GAGACTCCGTCTCAAAAAAAAAAAAAAAAAAACTAGCCAGGCATGGTGGTGT  
GTGCCTATAGTCCCAGCTACTTGGGAGGCTGAGGCAGGAGAATTGCTTGA  
ACCCAGGAGGTGGAGGTTGCAGTGAGCTGAGATCATACCACTGCACTCCA  
ATCCAGCCTGGGTGACAAAGCAAGACTACATTTCAAAAAAAAAAAGAAAG  
AAAAAGAAAAAAGAAAAAGAAAAAGAAATTAAGAGAAGGGCAGGTATTAA  
CCCCAAATATCCCACCATAGGGACACATTAAAGTTTGCTTGGCCACTCCC  
CTAGCATAATATATGGAATGTCTTCAAGGACCCTCTGTTGTAATACAAAG  
GCCCTGCTGGACTTAATACAACCTGCAGGCTTTGAGATCCCTACTCTGTT  
GCCATCTCTCATAGGATTTGCAGACCAATCCAAATACTTAAATAGCAA  
CACTCACAAACATGCAAAATCAGAGCAGAAAAGAACTTCTAAAGGCCCT  
GAAACTACACTTTATGAGAGAAGACAATAGGGACCTGAGGGTGGTAGAAT  
TTTCTCTCTATGCATCTATGTTTCCAGGGCTCACTTTCTCAATAAACTCT  
TAAATTGCTTTTAAAGTAAGGGAACAAGCAAAACATTACATTTAAGAGAAA  
TCAATTTTATAAAGAAGGGGGGATGTCCAGGGTACTTTGCTTCCATGTTT  
TGCTTCCATGAATTTGTGTTTAAACAGAAGATGCAGAAAAACACACAATTA  
TTGCAAAATCAAGGAAATCCACTCTAAACATCCCTTGTTTTCCAGGCCA  
GTGTCACAACTGAAAACACATATTGTGGCTAATTATGTGTACAAATTAG  
AATGACAAGGCAAGAAAAAAACTCTCTGATTAATAATAGCAGCCAA  
CACAGACAGCCTGTGTAGCTCGACTCTGCTGGTTTATAAAGGCAGAAGA  
AGCAAACGGCTTCTGTGACCGCAACAGGAAGGGCCTCTGCTCTTAATAAA  
TAAATAACATTTAAATTATTCTCCCCATTTGCAAAGCATTTTCCAACCTC  
ATTATCTCATCTGACCAGGTATTATTGTATCTGACCAAGAACTTGTATAC  
NAAATAAAGAATAAAAAATAAATATGGGCCANGCACAGTGGCTCATGCTT  
GTAATCCANCACCTTTGGGAGGCCAGGCGGGTGGATCACTTGAGGTGAG  
TAGTTTGAGACCAGTCTGGCCGACATGGCGAAACCCGCTCTCTACTAAAA  
ATACAAAAATTAGCCCGGCATGGTGGCACATGCCTGTAATCCCACTACT

FIG. 4 (22 of 61)

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TGGGAGGCTGAGGCACGAJAATTGCTTGAACTCGAGAGGCGGAGGTTGCA  
GTGAGCCGAGACTGCGGCCATTGCCCTCCAGCCTGGGCGATGAGAGCGAA  
ACTTCATCGAAAAACAAAAACAAAAACAAAAACACCTTAGAAGA  
AGCGTTCCTCCTCTTGCTTTCTGAAGACACTCTACGCTGAAACAGTAACT  
TTCAATAAACCATCTCTTCTCACCGCACTCTGCGACTTGCTTGAATTCC  
TTTGTGTGCAAGATCCAATAAGCCTCTCTTGCGGTCTGGATGAGAACCCT  
TTFTTTGGAATACTCTGACACAACAAATTGCAGAAAGAAAGTCTCACATG  
TATAAAATAAGCAAAAAGATTCTCTGGCATCTGAAGAAACAATTTCTTG  
TCAATATTAGTATCACTATAAGTGTAGAACAACCTGTTGTATGATGCTAC  
ATAAAGTATATGAATCTGAATACTGTTGGATACAAAGGGAGACTATNNA  
TGTAATACGTGCCCCGAAATGACTACACTGTTGGTGATCTTTCTTTCAAG  
AAGCANAATATTGCCTCNAACATCCTGTACATGGTATAAAATTTTA

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CCCAGCAAGAACACCAATACAACGGGGGGGGCGTTCTTTGTGAGGGGTGG  
GGAGGTCAATTTTTTTGGAACCTGCAGCAGGTAACACACAAAACTTCCACA  
GCTGCTACCAGCTTTCCAGGAGAGCCTGTGTACCTGGAGAGGGAAGGCA  
AGTGCTTCCGAACCTTGACTTGATGTCTTAGATTCTGCAATGCGTAGTCTG  
TAGGGACAGGCTGTAGCTTATCCTATAGGCTTGGGCTGGAGTCAGCAAGC  
ATCTGGGCTGGCAGAAGATAAAAGATGCAAAGGTGGAGGAAAGCATACGT  
GGTCTGGAAGACAGACTTGGTGGGTGGGTGGCTGCTACAACACCCCTAGTT  
AGAGGTAGAGGGGTAAGTCAGTGTGTCTTCTGCACAGGCCTCTTCCCCAC  
CTCATTCTTCATTTCCCATACAGCCTTGCTGAGTTATTCAAAACATCTG  
ATTCAACTGGAAGCTGGGTGAGGATGACCTAAAGGACTAGTGTGATGCC  
TGCCAGGGGTGTGGGCCCATAGTCAGAGTCCAGAGCCTCCTCTCAGCTT  
TTAGCACATCTCACCCACATCCTGGGTCTTAATTAGCAATATGAAAGCA  
AGCCAAGTGACAAGATTTTGTCCCTGGGAAGTCCAGAAGCACTCCTTTTC  
TCATTTGTATAAGCATAATGATTTGCTTACATAAATAATCATGAAAATTC  
AAATCCCTCTCAGAAATCAGGTCTATAAAACCATGAAATGCAGCATGTGGG  
CAAGAATCACAGGGAAGGTAGGTCTTGGAAAAGAAAGGATGGCAGGGAG  
GAAGAAAGCAGGGTGCCAGGGGCCCTGGGCTGCTGTCCAAGTCAGGTGGC  
TCACCGTCTCTGAGAACATTTCACTTTCTGGTAAATGGGGCAGTTGGAGA  
TAGAAGGGTTGGGTGAATGCCAAGAGTGAGCACAGCTGAGGTGAGTGTG  
TGCCCTGCAGTCCAGGCGGGAGTAGAAATCCTGGGCCCATCTTACCTCCGA  
CCTCATTTCCTCCTCTGTAATAATGTGGGGGTGGGGGAAAGTTCTGGTCA  
TCAGCCCTAGCAITCCATGGTTTCAATTCCTCATCAGTGATGGAAAATCAC  
CAAGCAAGAGAAACAGGATGGAGAATAACCGGATGGGTGCAATCGGAGGTG  
CTATTTCAAGGTGAGGTGGCCAGGGAAGGCCCTCTGAAAGGGTGGCTTGAG  
CAGGTGGCTGAATGTACAGAAGCTGCCAATCATGAAAGATCTGGGGTACA  
GCATGCCAAGCAGAGGAAATGCGAGTGCAAAGGCCCCGAGATTGGATGTG  
GGCTTAGCACAAATGTGGCATGGCAAGAAGGCCAGTGTGGCTGAAGCAGC  
ATGAACAATGGGTGGAGGGGCTGAGAGGACAGAGGAGCAGGAAAGAGCCA  
GGCTTGGGTAGGAGAGGTGTCAACTTGATATATGATGCAAAGCCCTTGGA  
GGTTCCCAACACAAAGCAATGATCTAATATATGGTTTTAAAAATGCCA  
CTCTTGGCCGGCGCGGTGGCTCACGCCTGTAATCCAGCACTTTGGGAG  
GCCGAGGCGGGTGGATCATGAGGTGAGGAGATCGAGACCATCCTGGCTAA  
CAAGGTGAAACCCCGTCTCTACTAAAAATACAAAAATTAGCCGGGCGCG  
GTGGCGGGCGCCTGTAGTCCAGCTACTCGGGAGGCTGAGGCAGGAGAAT  
GGCGTGAACCCGGGAGGCGGAGCTTGCAGTGAGCCGAGATTGCGCCACTG  
CAGTCCGCACTCCGGCCTGGGCGACAGAGCGAGACTCCGTCTCAAAAAA  
AAAAAAGAGTGAAGTGAAGCAGACCACTCAGGAGGTGAGG  
GCAATGGACTGTGCAGGAGAGACTGACATCTTAGACTCGGGCAATAGGAG  
AGAAGGTGGTGAGGATTATTTCTGGGCATAAAGGCAACAGAACTAGCTG  
ATGGCGTCAACGTAGGAGATGAGGGAAGAAAGAAATCAAAGGGCATTCA  
TAGGTTTGAGGGTTGAGTAACTGGGGATATTTAACAGAAATGGAGAAGTC  
TGGGGAAGGGGCAAGTATTGTGGGGGCGAGGGTCAAAAGTTCTGTATTT  
GGCCAAGTTAATTAATTTGAGATACCTCTTAGGTGTCCAAGTGAAGAT  
GTCAAACAGTCAATTTGAATACAAATCTGAATCTTAGCCAGGATGGTCT  
CACACCTGTAATTCGACACTTTGGGAGGCTGAGGTGAGAGGATCACTTG  
AGGCCAGGAGTTTGTGATCAGCCTGGGCAATAGAGCAAGACCTGTCTCC

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GATGTGTGTACGTGTGTGCAAATACCGTGCCTTTTTTGTTTTCTTTTGT  
GAAACAGAGTCTCACTCTGTGCGCCAGGCTAGAATGTAGTGGCGTGATGT  
CAGCTCAGCTGCAACCTCCGCTCCAGGTTCCAGTGATTCTCCGCGCTCA  
GCCTCCCAAGTAACTGGGATTACAGGCGCCCAACAACACGCCCAGCTAAT  
TTTTGTATTTTTAGTAGAGACGGGGTTTCACCATGTTGGCCAGGCTGGTC  
TCTAACTCCTGACCTCGAGATCCACCCACCTCGACCTCCCAAAGTGCTGG  
GATTACAGGCATGAGCCACCATGCCTGGCCAATACTGTGCCATTTTATTA  
TCAGGGACTTGAGCATCCATGGATTTTGGCATCCATAGGGGTCCTGTAAAC  
CAATACTGCACAAATACCAAGGGACAACCTGTATTGAAAAGACCAAAA  
TTAATAAGCAGGACGCTGAAGGTAAATGCCCTTAAAGTCATGATCCCT  
TGCCCAAGTGTCTGAACCTCAGCCAGTTTTTCATACTCAGGACCTATTGGCT  
GCAGAGGTGGTAGGAACCATATGAGAATCCTGCAATATCATGGCAAGTAT  
GCAGCTTTAATGATATCTGCAGTCCTTCCCCAAAAGGACCTTACATTTACC  
ATACTGCTATGTCTGCGTGAGAGGGTAATACTCAGATTTTTTTTTTTTT  
TTTTTTTACACAACGTCCTTACTGTGTTGCCCACTGGAGTGCATGGCT

FIG. 4 (24 of 61)

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CGATCTTAGCTCACTGC .CTTCTGTTT .TGGGCTCAAGTGATTCTC  
GCCTCAGTTTCTCTGAGTAGCTGGGATTACAGGCGCCCGCCACCATGCCTG  
GCTAATTTTTGTATTTTTAGTAGAGACGGAGTTTTGCCATGTTGGCCAGG  
CTGGTCTTGAACCTCTGACCTCATGTGATCCGCTGGCCTCCCAAAGTGCT  
GAGATTCCAGCGTGCGCGGCCATACCCGGCCGGGAATTCTTTATATATTC  
TGAAAACTAATCCTTTGTGAGACATAAGTGTTGTAAATATTGTATCCCAG  
TTTGTGGCATGTATTTTTAATTTTAAATGGTGTCTCTCAATGAAAAAGC  
TTAACTTTAAATGAGGTCAAATTGATCACCTTTTTATTTATGGTTGATT  
CCTTTGGTGTGATGTGTAAGGAATGTTGTTCTTCTCTGTCCTCAAGTTGC  
AAAGATTTCTGTGTATTTTGTCTTAAAGTTTTAAAGTTTTGCTTTTCC  
CATCTGTGCACATTTACATTTGCTACATCTCACTGACTGCTTCTCTGCTG  
TGCAGAGCAAGCTCCATGAGAGCAGGAGGCATGGGTCTGCTTCTTGTG  
GTCCCCAGAGCCCTATGTGATGACTAGGACCTGGCAGGGGACTAGTGAGT  
AGCTCCTGACTAACTGACTCAATGAATGAATGATTGGATGATTGAACAAA  
TGGGTATGGGAGTTACAGCGAGTAAGAGATGCCCTAGAAAGAGATGAAGA  
AGGAGATGGTATAGGGTAGTGGTTCTCAATTCTGGGTCCATGGTGGACTC  
ACCTGGGGACCCTTAAAAATGTACCGTGGAGGATCCAGCCCAAGAGATTC  
TGTATGACTGGTCTAAGATGTGGTCTGGGCACCAAGTGATCCAGTGTC  
AGCCAGGCCTGAGGCCACTGGATTTGGTGGTAAATGAGGTAACTATCAAG  
GGTACAGACGTTGGTTGCCAACAGGCTTGGGCTTGAATTTAAGCTTTGTC  
ACTGACTTGCTGTGTCCTCTGCACTCGTTGAGCCTGTTTTCTCAGCTGA  
GAGATGGGTGTGATAACACCTACCTGCTGTAGTTGTTGTGAGAGTTAGAG  
GAGATAAGCATGTTCTTGAATGAAGTGTTCTTAAATCCATCATAGGTT  
TTTTGCTTTGTTTGTGTTGTTTGTGTTTGTGTTTCTTTTCAAGAATGA  
GGTTGAGCCAGACTTTGACAGCTGGGTGGGAAGTGAACATGTGGTGATTG  
GGAGAGAAGGGCAGTTTATGTGAAGGGGAATGTAATAATTAGAGAGTGGGC  
GTGGGAAGACATGCTGGGGAGAGTGAGCAGGCCGTTAGCCCTGGTAGAG  
GGTGCAAGAGAGCAGTGCGGAATCTGCCAGGGAGACAGGTGGGTGACCAG  
GGTGCCAAGGGTGTGGCTTTTCCCAGGTTCCCATGGACACAGCCATCTC  
CCAGATGCCCAGCCTAGCTGTGAGTGAGCAAGAGTTCTGGATTGTCTCTC  
TCACTCTGTCTTTTTCTCTCATTCCAGAAACAAAGCAGTGACTGGTACTT  
AGGAGGAGAATCAGGTGAGTGGGAGAACTTGCTTCTGCTCAGGGGAG  
CAGAAGCAAGAATGAGGGCCCCACCATGCTGGAAGATGATGAGGGTTT  
GGTTCAGGGAGGAGGAATATTGGGGATCTAAAGGGGCTGGGAGTGGGGC  
AGGACCCTGCCTTAGGACAGGTAGAAACATTTCTATAAAAAATGGGGTG  
GAGGTTGATGGTAGGACCAGGCATCTTAGTTGGCTCCCTGGAGTGTC  
GCCCTTGAGATGGTCTTTAAAGCCATGCAGTGGGGTTTGAATCTGGTGT  
TCAAGCTCATAGGTTATTAAACATAATGACACTTGAAACTATTGGGAGA  
GCTCAAGTGAGTGGCTGGAAGTTCTGTGTTGGTGACGAGGTGACTTAG  
GATGTGCTGCTCCAGACTCATATCTTGACTGCACACCTGATGCTTCATC  
TGGCTATCCTGTAAGCACCTTCAACTTAACATGTCTACACAGAATCTT  
GATATTCCTGTTCTCTCCCCAGTTCCTCAGTTCCTTACCAAATGTTCTTCC  
AGTTACCCAATTGCTCAAGTAAAAATCTAAGTCTTCTCTTGGATTCT  
GCCTGTTCCCTCAACATCCCACCTATCCATGAGTGTCTGTGGGCCCTGC  
CTCTGAAATAAATCCTGCCTTTGTCTCCAGTTCCTCCAGCCACCCATC  
CTGGGGCTGCACCCTCCTCTTCCAAGCCCTCTCCCTTTCTTCTGGTG  
CTGCCTGTGATGTCAAGCATATGCATCAGTGGCAGGACATTTGAAAT  
GCAACCAGTACAATTGGGCGCGGTTATGCCCTACCAGTTTTCTTCTTAA  
ACATTTTATATTTATGTTTGAAGCATGCCACCTTTCTTCACTTGCCAAC  
TTGACAGATTTATTAGTTGACAACATCCGCTGATAGCATCAGTAATAAGT  
TAATTGTTTTTGCACATGTAGCTTTAATTATTCTCATTATCATTATAGG  
AGTTATTCTTTGTAAAGGGTAACTGAGTTTTCCAAAACAAACAGAAATTT  
GGGGTGGGCCCATGGAGCGTGACTCATGAAATCAGATTCTTAGAAGGACC  
TCGGCAAGTCTCTGGGTTGCTGTTAATGAGCCTGGCTGGCTGCCAGGGT  
GTGTCTGCCCTTTTATGAGGCCACCACTGTTCAAATGCTTGCTGCAGCAT  
TACTTGCTAGGTAGTGCTTGTGTTCTACTGAACTGTGAGGATCCAATTC  
TTTGTGGTCTAAGTAACAATACTCAGATTCACAAGGAATTGATTAATAAG  
CCAGAATGCCAATGTATTACATTTTGTATGAAGACCATATTTACAGTGAT  
TGTATCTGCTCAAGCTCAAATTAGGATTAGAGTTCTGACAAATACATATG  
TGAGAAGTATGAGGTAAATACTTGAAATTTGGACTTTTCTAGAAAATCT

FIG. 4 (25 of 61)

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GAATGTGATTGCCATTACATACCTTTCTGGGGATGATGATTCTTGTACT  
TTTATTTTAAAAAGACATAGAAAATACTTAAGAATCAGATTGCTTGGCT  
GGGCACAGTGGCTCATGCCCTGTAATGCCAGCACTTTGGGAGGCCAAGGTG  
AGTGGATTGCTTGAGCTCAGGAGTTTGAGATCAGCCTGGGCAACATGGTG  
AAATCCCCTCTCTACCAAAAATACAAAAAACAACCAAAA  
AGAATAAATTAGCTAGGTGTGATGGTGCCTGCTTGTAGTTCCAGTACTT  
GGGAGGATGAGGTGGAAGAATTGCTTGAGCCAGGAGGTGGAGGTTTCAG  
TGAGCTGGGGTTGCAACAGTGTACTCCAGCCTGGGCGATAGAGTGAGACT  
CCGTCTCAAAAAAATAATCAGATTGCTTTATTGCTGGTTTTCTTTCT  
AAAACAGATTGGGTCCCATCATCCCCTGGCCCCCATTGGTTAATGGTT  
CCTCCTTTGTCTATTGAATAAAATACAGATGTCTGCTTTTGGCAACATGG  
TTGAATGTAGACACTGCAGGGTCTTCTGACTCAAAATGATTTAGGCTTA  
GATAAACACATTTGGAATGCATTTCTGGATTAAACCAAGGAAAGGAG  
ATCTCTTTAAATCCCCTTTCTGTTCCCCCTCCCTACCCCTCCAATTGG  
GCTTAAGTAAGAAGGGTGGTTACCCGCTAGTAAACCCCTTCGAAGGGGG  
TCTTCTCTTAAGGGAAACCTTGTTTTGACATTTGCTTCAATGGGCC  
CTTGATTTTGTTCCTTGCTAAACGGGTGCTAAACCAGGGCCTCCTCTT

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AAGGCTTTTAGAATATTTGCACACTTTAGAAATGGAAATGTTTTTGGGG  
GCGAGTTGTCTTAATATTTTCTAGCTTGTGTGACATCCTTTTGA  
AAGCAGCAATTCCTGGCCTTTGTGAGAGATGGTGAATGCCTGCAGGTGTGT  
GGACCAGTGCCTCCCTTCTTCTACATGCACGGCCCCCAGCTGGGCCCCA  
GCAGAGTGCTGTTACAGAATAATTTCCAAGGGCTGTGTCTTAACCTTTG  
GTCTGTCCCCCATTGCTGTAGATTGGCCAATTGACTTCATAAGTGCCT  
CTTATGAACATAGATGTTGGCAATGGAAGTTGAGGACCAGTCAGTGGTTG  
TTTTATTGAACACACAGCGTAAATCCCAACACAATGCTGACCTAAGAGAA  
TTCCAGCCACTCTGATTCTCAGTCTCTTTATATCTGAAAGGGTTCTGTTT  
CACTTTTTCCAGATCAAAATGTCCCTGCAGCTACTCAGCAGAGCTGTGCG  
CAACTTATACGTAGAAGAGGTAACAGTCCACAAACAGAAAGGCACAGGAC  
GAGAGTGGTCTGGGTGATGCTTCTGTGGGGGAAAAGGTGATGAGGGTGC  
ATCTGCACACCTATGTTTCATAGGTAAGTCTGGGAGGAGGTGACCTCCCCT  
TTGGTTGAGGTGCTGAGGCGTCTTGTGTAAGTGGCACTATTCCATTATC  
TGATGCAGTCTGTGGGAATTTGTGGTATGGCCACCACAGGTACCATGCT  
GGGAACAATGCCAGATACTGCCTGCTAAGCCACAGCATGAGTCACATGAG  
CATTTGTGGGCTTTGGGAACTAAAGTTATTGAACGATAGTTATCTGAAAA  
GGAATTTAGGGAAGGGGACTTTAGTCCAGCGAACAGTTTGCAAACCAGG  
GGGAAGGCAGCCTTCAGCGTAAATGAAGACGTGTGTGCCCCAAATAACA  
AAGGGAGAGTTTGTCTTTAGAGAGTAAATGTCCACGCAAGGTTCCACTT  
AGGCAATGAAAGATGCAAACTTGCTTAGTTCTGATTTGTTTACATTGTC  
TGAATTCGGATTGGTCCGTGCAGGCTTTTCTGGGAACTCCAAATACATGT  
ATGACCTCTAGTCATACATGGCAATGGCCGCTTGGCTCTAATTTGAATT  
TAGGCCCAGTTAGTCACTCAGGATTAACCTTTTTTCAAGGTTTCAAGCTCT  
GAACAATGGACTTAGACCTGCAGGACATAATCTGTTTCTTAACCTCTGGGAC  
TACCTGTGCTTTTGAAGTGTGCCCAGTGAGCAGCTGTGGCTCTGGGCCCCA  
GACCCACAGGGCGATAAGGCACAGAGGTACGCATGGAGCAGGCTGTCTT  
GCTGAGTGATCATGAAGATACACTTACATAGAGCAGCACTTTTCTTCCA  
GTCTTTGTGATTTAACTCATTAGATCCTTATAACAAGAGTCAGTCTCTA  
TTTAACCCATGAAGCACAGGTGGAGTCCAAGCTTAGTTTGTGAAGGATGA  
GCCAAAAGGATTCTTCTTGTAGACCTCAAGCTCAGCTCTCTCCATGGG  
CCCTGGAGTAGGTGAGAAGGCCTCTGTCTTCCAGAGCCCACTGCCAATCA  
TCTACATTTTCTGTTAGCCCAATTCTAGGACATTGCTTTACCAACTGAAG  
GGTGAGAATATCATAAGTTATAAAATCAATTGAAAAACAAAAGGTAC  
AGAACAGAAAAATAAAGATGAGAATCTATTAACATAGTGATGTTACTGG  
AAAAGGGGGTCTCAAACAGACCCCAAGAGAGAGTCTTGGATTTACAC  
AGGAAAGAACTCAAGGTGAGTTGCAGGGTGGGTGAATTGAGAGAGTTTA  
TTGAAAGCTATTCCATTACAAAGTAGAGCATCCTCAGACAGCAAGTGGAG  
GAACATGCCATCATTAAATTTTCTTATATAGGAATCTTGTCTATATAAA  
GACTAACTAAGCTGTGGCTATGTGTGGGTGGGCCGACAGCATGAAACA  
TTTATTCTCTATTGATTTAAAGAGAACTATCCTTGACATTTTAGTGTGT

FIG. 4 (26 of 61)

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TTAAGTACATCAAAGCAAACTATAATTA:CTTGAAAGCATATATTTTAA  
TAGGGATTGGGACATCTGGGCTTTCTGTTGTTGTAGAAGTTTGTCTTGC  
AGGGATTACCAAGCCACTTCTTAGCTGTAAACATCTTAGGGCCATGGGT  
CCTGACTGGCAAGGAATGTGTCTTGCTAGTTTAAAGATGGGCTTGATTG  
AAAATGGTGTCCATCTGGCTCTCCTAGGCTCCTGCTTCTTAACAGTAAG  
GGTAAATGCTATGTTATGAAATGTCAATTTCTGCCTTTAGCTTGCAAACCT  
TTGATGGTGAAATTTCTCCTGTCCGTTTTAGTGGGGTATTTATTCTGCAT  
CCACGTCTTCACAAGGAGCTGAAAACAAATTTGGATGGAAGCAACTGGGTT  
TTATGGGACACGTTAATGTTTTAATGTCAATTTGGTGTGGAATTCAGATGT  
CCAAGCAACATTTTACACTACAAATCTGCAACTTTAATAATCACTCAAAG  
TACCTGAACCTCAATGCTTTTACAGACAGACTTGGTATAAAGCCACCACCTC  
TTTCTATTATGGCAGCCCTATCCTGAGGACACAAATTTCTGCAGGGCTTC  
TGGCATATCTCTGATTAAACAAATGTCAACAAGGTTAAAACAAATGTCAT  
CTCTGATTTGTTTGTTTTAAAGCCTGGATTTACTCATTGAATATTTCACT  
CCTACTAGCATGTCTTGTAGTAGTTTTCTTCAGGGACCCTAATTATTGCT  
ATTAATAATATGTGTGCAGCTACATGTTTTTTTTTTTATCAATTTGCAATG  
AAAACCTTTAATTGAATAATCTATTAGTGTTATTATTGAAAGTGAAATCT  
TTTCCTTTTGTCTTTCTTCTTCTCACACATAGTGCAGACAGTTTCCACAG  
GGCTCATAAAAGGAATGATTCTGCCTTGTGTGAACCTTTTGCCTTTATTG  
TTAATTGCACCATTTTGTGACTGGCTTCTTGACCCTGTTGTAACCAAGCT  
CATAATGTACATTATTTCTTATTTTGCAGTTGTAGACACTTGAGGAAGTT  
CCCATCTTTGTTTCTTCTTCTTGTTCCTGTGATAACTTTTTTCATG  
CAGACATTTTTTTTTTTTTTTTTTTTGGAGACCGAGTCTTGCTCTGTCTC  
CAGGCTGGAGTGCAGTGGCATGATCTTGGCTCACTGCAACCTCTGCCTCC  
CAGGTTCAAGAGATTCTCCTGCTTCAAGCCTTTCTAGTAGCTAGGATTGCA  
GGCGTGCACCTACCACACCCAGCTAAATTTTTCAAATTAGCCACCCACCT  
GGCTAATTTTTGTATTTTTTAGTAGAGACAGGGTTTCAACCATGTTGGCCA  
GGCTGGTCTCGACCAGGTGATCCACCCGCTTAGCCTCGCATAGTTGCAG  
GTGCTATTCTGAGCTCAGGGCTCTGGCAGCTACAAGCCCAAGATGCGGTC  
TCCAACATGTGGCCATTCAATGTCTATGGCGCCCTCTACTGGTCTGGGAA  
CGCAGCTCTGCCAGTAGCTCCAGCAGGGCACAGCTGTTAAGTCGTGATG  
TTCTACAGGTGACCAAGGGCAATCTCTGGACTCCTTAGCCGCTAGGTCC  
TCTCTGTAGCAGGACCCAGGAGAAGGCAGGGGCTGAGGATGGCTCTCTTA  
GACATTTGTGATGAACCAAACGTGTGCATTCTGAAACTTCTGTGAGCAA  
GCAGGTGAGTAGAGTTGGGTTATAAAAAGTCTTAGGGTCTCACTACAGAG  
ATGGACTTGCTGTGTAGATGGTGCAGAGCCGCTGAAGAGTTCTACTTGGG  
GTAATGGTGTGATTGGGTTTGCCTTTTAGGAAGATTCTTGGCCAGAATG  
AGCGGGGCAACCCAGAGCAGGGAGTGGCCACATGTGGGTGTGCAGTTATG  
GGCCACTAATCCAGGTGATAAAATGGTGTCTCTGAACCTCAGGTGGGGTG  
CCACATGTCTCCATCTGCTCTGTACCTTTGAGACTGGCCTTATGGGCTGC  
CTTAGTGGTCTGTTGTCTCTATCTCCTGGTTGGGCTCAGGCAATGGGAG  
ATCAGAGGGAGGAAAGAGAGCTTGGTTAGAGTGCACCCGCGCCCTTCAG  
GTTGGCAGTGGCCACATTTCCCTATACAGAAGGCCACAGTTTCTGTCACT  
GGCCCTCCACAGCCCCAGCTTTCTCAGTGGGCCAGCCACCTCCCCATCC  
CTTGCTCCTCCTCCTCCAGAGAGGGTTGTGGATTTCCACTGTCAAGAGTG  
CCTGGAGCTCCACCATCTCCTGCTGCTTCTCTGGACCTGCCTGCAGTTT  
TATAAATAACCTTTCTTACATTACCTCTAGCATGCACCTTTTGTGTGTA  
TACTCTGCCCCCTGTCAACATGACTCATGCCAAAGAGTTTGAATTTTT  
TTCTCCAGGCAACGGGAGGTCAATTGGAGGATTTTAGACATTGAGAACAGA  
TGTGTATTGTGGAAATATCTGTCTGACTGAAGTGACCAGGATGGTCCAAA  
AGAGCGAGAAATTTAGGCAAGCAAACCATCAGCAGGCCAGCAGCAGAAAT  
CCAGGTCAATAACAGGGAAGCTGAGGCTCACAGGGTTGGATCAGGGAAATG  
GGAGAGGGAAGCCAAACAAATTCATGAGCATGTCAATTGCACATATGACT  
TGGTAACTATTTTTATTTTTATTTTTATGTTTTGAGACAGAGTCTCGCTC  
TGTCACACAGGCCAGAGTGTAGTGGCATGATCACAGCTCTCTGCAACCTC  
TGCCTCCTAGGTTCAAACAATTTCTCCTGCCTCAACCTTCCAGGTAGCTGG  
GACTACAGGTGGCGACCACTACACCCAATAAGTTGTGTATTTTAGTAG  
AGATGAGCATTACGCTGTTGCCTTAGACACGG

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AATATTGATTATTTGACCAGAAATTCATGCAGCTAACCCTGACCCCTGGC

FIG. 4 (27 of 61)

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AAAATAAAATAGTGTAT...GTACGTGCATATACATGCAAAGAAATGAGI...  
GAAACTAGAAGGATGTCAATCAAATGATAACATGGTCATCTTGGGGTCGG  
AGTACATTTGGGGATGAGGGGAGCTGTAAAAGCAGACTTGGACCTTTTCT  
TCTACCAGTACCGTGTCAATTTGAATTTTGGAAAGAAAAAACTCAG  
AAGGAGGAGAAGGAGCAGGAGGAGAAGATGGATCTTAAGTGATTGTC  
CCGGGAGCACCTTGAGAAGGTGAGATTCAAGTCTAGGTCTAAGCTTTCTA  
ATTCCATGAGTGGGAGTGACCCACGTCCAAGAGGAAGCTCAAAAGGAAGA  
TGTTCTCCATCATCTCTTGCTCATCCTAACAGCATGCAAACCATCCA  
ATGCAGCTCAGAAAACCTCCCAAATTGCCAAATTTTATTGGAAACACTTAA  
TGCTGTGGTTTCCAATTTCAACTGTAAAGTAGGTATGTATGCCATTGTTA  
CCATTAACTTCTCAGAAATGGAGAGAGCTCTCTTCCGCCTCCTCCCCCT  
CTGCTGTGGCTTTGGTGAGACGTGCACTCAGGCTCACCTGTCTCCATGAT  
CTCCAGTAAGTACACATGAGCAGAGAGGCTCAGCTCAGCTCTTCTGGT  
CCCACCAGGGTTGATTCTTTGAGAATTCTAGAATGCCACATCCTAGGCCC  
CCCAAAGAAATCCTGCATCTTACCCCCAGAAATATGAATCATAGCAAATT  
TCAAATCAACCATCGTTTAATACTCACAGACTGGGCACATCCAAAAACAT  
ATTTTCAGTTTTTACAACAGTGCCTGGTGCATATCGGCACTATTGTGGAA  
GCAATAAATCGACACGGAGCTGAAACACAAACAAATGCCAAATGTTTT  
ATAACACCTGATTTTCTTCTGTTTCTTATGCAGTTAGTTTTGTTTTG  
CTTAACCTCTACCTCAGACCATAGTCTGGTAAACTCACCACCCAGAAGCTC  
CCTTGAAATGTGGGTATGCAGCCACTAGGTGGCAGGAGAGATTTCTGC  
CTGGAGGGAGGACAGCCACTCTGTCCCCGGGTGAGGCCAGGGCCACCCTG  
CTACCTGCAAAATTAGCATGGGGCTTTATGAACACAGCTTCTAATAAA  
CACAGGATCTGTTTATAGAGACTCCAAACACGCCTACCTAGTGATGAA  
AGACTCAACTTCAGAGAAAACCTTCATGGCAAACATCTTCAGAGATGTT  
TCCAACTTAAGGTTCTGAACACAGACGCTTCCCCAGAAAGCCATTGTTT  
TCAGCACCTGGGAGCCTTGCTTTGCTTTGCTTACAGACTCGCTGTTCTTA  
AATCACTGCCAAGATAACATCTGTCTCTTCTTACCCTCTATTTGATA  
TAAGGACTCCTCACTCTTGTTGCTTCTATTGGCTACCTCTCCACAGGGA  
GAAATCGCTGATTTAAACAGCAGTCAATATCCCAAATCTGGAACAGGGAAC  
AGGGAAGCATTTAAAAATTGGAGAATTTAGGCCGGGCACAGTGGCTCATG  
CCTGTAATCTCAGCACTTTGGGAGGTGACGTGGATGGATCACTTAGGAG  
TTCGAGACCAAGCCTGGGCAACATGGCGAAACCTCATCTCTACAAAAAAA  
AAAAAAAAAAAAAAAAAAAAAAAAAACCAGAAATAGCCGGGCATGGTA  
GTGCACACCTGTGAGCCCCAGCTACTCAGGAGGCTGAGGTGGCAAGACTG  
CTTGAGCCCTGAGGTGAGGCTGCAGTGAGCCGAGATCACACCACTGCAC  
TTCAGCCTGGGCAACAGAGTGAGACCTTGTCAGATAAAATAAATTAAT  
TAATTTAATTAGAGGATTTAAGGATTTTCCCTACAGACACCTCCTTATTT  
TCTCTGGCCTTTCTGACTACTCTCCCTAACTCCCTGCTCCTCTGGTCTC  
CCAAACTACTCCAGAAAAAAAAGGGGGGGAGGGACTAAAGGAAAGCC  
AGGTGACAGTGCCAGTGTGACAGATGACAAAGCATCTGCCCGAACAAACC  
GTAGGTCCCTGAACCTTTCTCAAGACCTGTCTGTGGACTTACCTATGAAA  
ACCAGTTTTAGCAAAAACCTCCTAAGCCAGTTTATCAAGATCCCCCTTAT  
CCTCAATATCCATCTGATTGGATTCTTCATCCCCCACCATTCCCCAGTGA  
TGTCACCAGGCCTTTCTCAGCAACAGTAGTTAGTGGGTGTAGCCAGGAC  
GCCCCCTCACCCCTGATATGCCCTTTTAGTAATTCTTCATCCACAGGTTT  
CCACCTTGCTCCTAGGCTATACATTCCATTGCCCATGCTGCATTGCGA  
ATTGAGCCCAGTTCTATACTGAGGTCTTACTTCACCTCTCGCCATAGTCC  
TGAATAAAATTGGTTTTACATTTAAAACTGTCCAGCTCTGGTTGTTCC  
TTGACACAGGGTAATTTTATTCCATGTGATAGTTTGCTTACCTCAGCC  
TACACCCCTCAAACCTGCAACTCTATATTCAAGAACCAGACAGCCCTTC  
CAACAGATAGGAAGAGGCTGCCCTGGTGCAAAGGAAGAGGCTCTGGGAGG  
AAGGAGAGAACCCGAAGGCTGCCCCCTCCTCTAGACTGAGCTCTGGGATG  
GGTGGACGATAAAACCCAGATACGTTTAGACATCTGAGCGTGGAGAGGAC  
TTTGCTTTGCTTCCACAGGGACCCCAAGGAACTGCAAGCCCTCCAGAGA  
CTAAAAACAGCAGAACAGCAAGAAATGGCAGCAAAGGTCTGGGCAGAAATC  
ATCCTATGTGGGCACAGACACAAACAGAGTCCCCTGTGGCCCCAGGAGAG  
TTTAAAGAAGATCCAGAGGCTGTCTATTCCATATCTCAGCAGAGACAGG  
CCCCTGAGCCTAAAAGCTGATCATTAGGACAAGAAGGACACGAACGTGCTC  
TGCAGCGTGAACCGCTGGAACAAGGCCAATCACCAGACACCAGACCAGC

FIG. 4 (28 of 61)

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CAGACACAGCCCCGCGAGTCCCCAAGACACCACGGACCCATCGCCCCCTC  
ACCAATAGCTCCAGGCTACATAGACCCCCTCCACTTCATGGATGTCCTCA  
GAGCAGAAAGGGGAGGCAGGAGTGGAAACCCTGACTTGGTTTCAGTTGAAAC  
ATAAAATGACTGTACTATTGAATTGCTGAAGTTTACGTGAAAGAAAT  
GAGATTTAGTTTTTGGCCACAGTGC AAAATAAGAAACGAGGCTTCAACTG  
AGATTAAGGTGAGTTATAGGAAAATGTACTCCCTTGAAGGACCTGTGAAG  
TGTGTTGCTATGAGAAAATGACCAGAATCCACGTTCTTAGCTGCGGGAC  
TCAGGCTGACTCCTGTTTCTGGAGCTTGCAAAAGGGCAGGGAAATCCCT  
GTTTCAGGCACAGTGATTTCAATGTTTAAAAGAAAACAGGTGGGCCCTGG  
CAATCATGATAACATGTCATAAGTTTACATCTCTGTGAGGCAGGTAGTGT  
AATCCCCATTTTGC AAAAGGAGGAAACCGAGGCTGAAAGCAGCTACATGGT  
CTCTTCAATGTGGCCCAAATGTTGGAGAACAGAGCTTAACTGAATCAGCA  
ATTCTATACTTAGAACTGACTCTCTCTTTATTATATCTCACTACTACCTT  
GATATTTGAAATATTCAACTTTTTTCAATCAAAAAATAACAATAATTTAG  
GCATAATGACTACTATGTCATTTAATTTCTTGCTGATATTTCAATATCCC  
ATGCCAGGAATATTGAAAGCTCAGCTCCTTAAGAGCTGACTATGGCATCA  
ACTCCCAACAACCATCCTTCCAGAAATATTTTCCCTTTCTTTTGTTATA  
GAGTGGCACTGCCCTATATGGTGACCACTTGCCACATGTGGCTGTTGAAC  
ACTTGAAATTGGCTTGTGCAAAATTGCAGTGTAAGTGTA AAACACATAACC  
AAATTTCAAAGACATGGCACATAATAAAAAATGTAAATATCTCATTAAAC  
AATTTTTATATTGACTGTGTAAGTAACATTTTGAATATATTGGATTAAAT  
ACATGGATGATGCCCCAACCCACAGTCCCTTATCAAGTCTCTACTTCA  
CATTTTTGTACTTCTGACTTAGAAATAGCACTGGCGTCTAAGAGCCTATT  
AATGTCGTCAATAGGTTCTTGGGAACCAATTTTAAACAAAATGACATA  
TAAGAAAACGAATAACATTGAACAAAATGACATTATTCGAGGACCTGCTG  
CATGTTGTTTCACTTAAAGTCAGTGTCCAAGAACCCTATCAGTGACATTTA  
GTGAGGACTTGCTGTCTTCTGTTTACAGGAACCTGGGCAAGTTACTTA  
ATTCCTCTAAGCCTGGTTTATATCCCTGCAAAGAGAGAAGGATAATAATC  
ACCACTACTTAGTGATGTCGTAAGGAGAAAATAAAATAATAATATGAAA  
TGGCTGACAGTGTCTTGTACACAGAAAGATGTGTGATCCACAGTAGCTG  
CTATTGTCTGCCTCACTTCACTAGTAATGGTCCAGGGAGGCCTTTAATGT  
GCAATGTCAGTACATTACATGTTGGACATGGGTGAAGGGAAAGACCAG  
GCTCATCTAAACACAACTAGGATGCTTGTGGTGTTTTGAGGAGGAATCAAG  
GACTAGTTATCCACAGCTGTAACATGCATGGATCAAAAGAGATAAGGCAC  
ACAAAAGACTTTGTGCTAGCAAGCATTACAAAATGCAGAGACCAGCTG  
TGGGTGGTGGTGAGTCAGACCCAGCTTCCCTCTGTGCCTGGCTGAGTGGT  
TCTGGGCAAGTCAGGCCATCTGTCTTGATGCCCTTCCCCATCTATAGAGA  
GGGAGCACTGAGGCCCTTCCAATACTGAAGTCTTTATTTCTGCTACT  
TTAGAAATATCCACATTTTGGTAAATTCAAATGATCCAATGATTCCATT  
TCCTAATGTTCAAACACTAGCCCCAGAAACATCTAAATGAATCAAACAAAT  
AAAATATTTATTGTGTATGTTTTGATTGCTGAAACTTCTATTTTAGCAAC  
ACACACACACACACAGAACCCATAAGCCTTCATCTTCTTGGATAAA  
CGAGCCTTCTGTCTGGCCATTTAAGTCACGATTAAGTAAATGATTTCCA  
ACTCGCCTTTTGACAGAGTTCAGATGGGTCTTCTGCGTGGCAGTGGCC  
CTCCTGACTTATGATTTCTGTGTGTGCGCCTGTTACCACTGCAGCTTAA  
CTGAGGAAACAAGAACAACAGCTTCTGACCCCAAGAGACTGTTGGAGG  
CAAAGGCTTCACTCCCAAGAACCTCACACGTGGGGAGCCCGAGAGCCAG  
CCCTGACCTTTTCTCCAGTAATAACATAAGAAAACAACAGGCACTGGCCTT  
ATTTTGGATACAAAGAGTGGTGCTTTTCTTAAATCTTCTTTAGTCAGG  
GCTACCCCTTCATGGACGCCCCAACATCCATGGTTCTGCTTGAGTCCCT  
GCTTCCATATTCCTGCATTTCTCACTTGAATATCCCTGGAGTACGTAA  
GCAGCCAGGTTTGGAAGTCTTGCTGTGCAGGCGGGTGTGTGCATGTCCT  
CTCTCTCAACAGGACACAAGCTCCCCAAATCAGACGGTATGCCTCCACGC  
CCCTTCCCAAGCCTTCCAGCAGCACCGAGCATGTGAGGGGAGCTGGGGC  
CCAGGCCATGATGGGAAGCACTCTCTGCCTAAAGACTAGGGTGTGTCGCC  
CTCAACTGTGGSAATGAGCCCCAGCTCTGGTGTCTGCCTCGGTTTTTCT  
CCTGGACAAATCAACATGAACTCCTCACCCTCTTATCCACTTTGCATAAA  
CTGAAAATAACAAACCCAGGGCTCTTCTGTACAGGAAAGGGTTTTTTT  
TTATAAAATTAAACAGAGATGATTCACACACCCAGGATATAACACATGG  
GCCATGAATCAAGGGCAGCATTGCTCTGGTCAGCCTGTTGTTTGGGCCCC

FIG. 4 (29 of 61)

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CTTGGCAGGGCTCTCCCCGAATCTTCCCCCTCTTGAATCCCATCANACA  
GCACTCCANCTTTGTGTTACAGGCGATAAATGGGAAAGGGTAAAT  
>Contig48  
CATTCTTAATTAGAGAAACGCTCATTAACTAGACACCCAAATCTCTGG  
GGGGGATCATTCTTACAAGCATGCCCTTCTCTCTTAAAGAGAGCACT  
TTTTTCGCAAATAATGCTGCCATGAACATACGGGGTGATGTATCTTCGT  
AATAGAATGATTTCTATTTTGGGGGGTATGTACCCAGCAATAGGATTGCT  
GGGTCAAATGGTATTTCTGGTTCTAGATCTTCGAGATCTTCCACACCGTC  
TCCACAATGGTTGAACTAATTCACATTCTTACCAACAGTGTGAAAGCAT  
TCCTATTTCTCTGCAACCTCGCCAGCACCTGTTATTTCTTGAATTTTTAA  
TAATCGTCATTCTGACTAGCATGAGAGACAGTATCTCGTTGAGGATTTGA  
TGTGCATTTTCTTAATGATCAGTGATGTTGAGCTTTTTTTCATATGTTTT  
TTGGCTGCAAGAATGTCTTCTTTTGAAGAAGTGTCTGTTTATGTCCTTTGC  
CCACTTTTTAATGGGGGTTTGTTTTTTCTTGTAAATTTGTTTAAAGCTCCT  
TATAGACTCACAATAACAAAGACATGGGATCAACCTAAATGTCCATCAAT  
GATATAACGGATAAAGAAAATGTGGTACATATATACCATGGAATAGTATG  
CAGCCATAAAAAAGAATGGGATCATATCTTTGAAAGGACATGGATGAGC  
TGGAACCATGATCTCAGCAACTATGCAAGAACAGAAAACAATTGTTG  
CATGCTCTCACTTATAAGTGGGAGCTGAACACTGAGAACACAGGGACACA  
GAGAGGGGAACAACACACATTTGGGGCCTGTGAGGGTGAGGTGGGGGAG  
GGAGAGCATTAGGAAAAATAGCTAATGCATGCTGGGCTTAATACCTAGGT  
GATGGGTTGACAGGTGCAGCAAATCACTGTGGCAGACATTTACCTATGTA  
ACAAACCTGCACATCCTGCACACGTACCCAGGACTTCAAAATAAAGAGA  
GACAATACTTCTCCCTTAAGTGTCTACTGTTGCTTTGCAATAAAAAETTC  
CTGCCCTTCACTTCACTCTGACTTGTCCCTGAATCTTTCTCGTGATGGT  
GTCAAGAACGTGGACACTGGCTGGGGCTGGAGACTCACCAGCATCCGGAG  
ACCCTCCTGAGCCCTCCAGCAATACAACTTTGACACAACTATGAAATCA  
CAGATCCAAGAAGCTCAAAGAACCCAGCACAGGAAACATGATGAACTA  
CATGAAGGAACATCAGAATTGAATTGTTCAAAATCAGTGATAAAGAGTAA  
ATCTTAAAGCAACCAGAACAAAATATCCATCATATACGCAGAAATAAG  
ATAAGTATGACAGCAGATTTACAAATAGAAAAAAAACAAGTGCAGCAAC  
AGAAACAAACTATCAATCCATAATTCTATACCTAGTGAAAATTTCTTTCA  
AAACAAAGGTGAAATAAAAAAATTATTTTCAAGGAATACAAAAGCGAAAA  
ATTAATCACTAGCATTCTCACTGCAAGAAATGTTAAAGGAAGTCTTTA  
GGCAGAAAGAAAATGATACAAGGTGAATATTTGGATCCCTGCAAGGAAT  
AAAAAGATCCAGAACTGATACTTAATGGGTAAACATGTAATTTTCATCA  
ACAAGTGAATGAATAAACAATCATGATATATCCATATGATAGACTACTA  
CTTAGAATACAAAAGAAGAACTACTTATGCATGTGATAACATGAATGATA  
TTCAAAATTATTATTGAGTGAAAGACACCAGATCAAAACAAAGTACATAC  
TGTATGATTCTGTTTATATAAACTCTATAAATTGCATGCTCTTCTATAG  
TGACAGAAAGAAGATCAGTGGCTGCCTGCAGACAGGAAGAGATTACAAAC  
GGAAATGAGAATTCCTTAAGAGATGATGGACATGCTCATTACCCATCATA  
TGTATACAGCCATAATGGTTTTACAGATACATATATGTACAGCCAAC  
ATAAATATAAGTTATCAAATTACAGTAAGTTCTGACTTAATGTCACTAGG  
TTCTTGAAACTTTGACTTTAAGCAAAATGATGTACAGTGAAACCAATTT  
TACCATAGGCTAATTGATATAAAGATGAGTTAGGTTTTTGGTTTTTTTTT  
TTTTGACATGAAGTCTCGCTCTATCGCCAGGCAGGAGAAGAAGAGTTAG  
GTTTTACAGCATGTTTCTGGTCACAAGAACATCATCAAACCTGTAAATAA  
AGGCACAAAACACTTCTAATATTAAATATCAAAATAAATATGAGTTATAC  
AGAATTTAAGAAAGATTATAAAAACAAGTAAATCATTATTTATGGGAT  
TTTTGGTAATCAGTGAGTTATGTGGTCATAGTGAAGTGGGTTAAGTCAA  
GAAATAAATGTTTGCAAAACAAAATTTTAAAGATCCTCTCCTACCACCA  
CACAAAAACAAGAAAACACGGTGGGCTCGCTAAGCACTTTTGTACCACT  
CGTATCTTATGCGTTTTGTATGATTATTGTAAATGCTTTATGATAATTTTT  
AGAGACAGGGTCTCACTCTGTGTCTCAGGCTGGAGTGAAGTGGTGCAATC  
ATAGCTCACTGCAGTCTCAACCTCCCGGATTCAAGAGATCCTCCACCTC  
AGCCTCCAGTGTAGCTAGGACTACAGTTGTGTGCCACCATGCCATCTAT  
CTTCTTTTTTATTTTTTGTAGAGACAGGGGTTGTGCTTTGTTGCCAGGC  
TAGTCTTCAACTCCTGGGCTCAAGCAATCCTCCTGCCTCAGCCTCCCAAA  
ATGCTGGGATTTCCGACATGAGCCAGCAGCACCTTGCCCAGCATTTTATT

FIG. 4 (30 of 61)

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TCATAATAATTATAAGTCATTCCCTTCATTTCATCTTACAACCCACTTGTTTC  
CAGTTTCAGGATCTCGGGTGACCAGAACCTATTAAACGTTTCACGCACAAGTC  
AGAAACCAGCCCTGGACAGGACACCATCCTACCGCAGGGAGAAGTTACAC  
ACCCACACTCACTCAGACTGGGACCATGCAAAGAACCTAACGTGCACCTTT  
GGAATGTGTGTTCCATACCCACTAGAACAGCTAAAATTTAAAAGACTGAC  
CATACTTGAGTGTGTAACAGGATGTGACACAACCTAAATCTTTTAAGCGCT  
TCGCGTAAATGGCACAGCCGCTTTGGAAAACAGTTGGCAGTTTTTCAAG  
TTAAATATACCCAACTCTATGATCCACTTCTCAACAATCAAACAAGAGA  
AATAAAAGCAATGTCTACACAAGATGTATACACAATGTTTCATTGCAGC  
CTTAATTATACTAGCCCCAAGTTGAAACAAGCCAAATGTCCATTACCAGA  
TGACTGGAACATACAAATTGTGGTATATTGATACAATGAAATACTACTTA  
GTAATAAAAAAGAAAGAGCTATTAACATAAGCAACAACATGGATGAATCT  
GAAAACAATTATGCTAAGTGAAAACAGCCACACAAAAGTTACATACTGTA  
TGATCACATCTACATAAAATTACAGAAAAGGCAAACCTAATCTATAGACAG  
AAAAGCAGATGAGTGGTTACCTAGGGATGGGGCAGAAGGGACGAAAGGAT  
GGATTGCAAAATAGCACAAAATATTGGAGGGATGACAAATATATTTCATT  
ATCTTGATTGTGGGGATAGTTTAAATGGGTATATATAGAGATCAAAGCTCA  
TCTAATTATACACTTTTAAATATATGTATTTTCATTGTGCATCAGTTATTCA  
TCAACAAGACTATAAAATAATATATGCCTACATACATTTTTTAAATATTCA  
AAATCTCACAGTTATATACATAAATGCAACTGAATATGTATTTCAGATGTT  
TTAACAAGCAGAAAGGACTGATTAACTCATGACAGCGGCTGTTTCTGGG  
AAGGGTGTAGGAGACAAAGAGATGGAAAAGAGGATGAGAGCCAGAAGAGAC  
CCTTGTAATGTTTCTTTCTTTTAGTAAAAATATATTGACAGTTAAAGCT  
GAGAGGTGAGAATAATAGTCTCATGGCTTTTGTGTCCTTAAAAATTCACA  
AACTAAGTGAAATGGGAGAAAGCAAAAAATAAACTTAAATAAATGTTAT  
ATTGCCCAAAAAGAGATTTAAATGGAGGTTAGACACATGAGACTTACGT  
TCTCAAAAAGTAGAATCTGCAGGGAAGTTTAAACAATAAAGAATTAA  
AATCTAGCTTCTACCAGCCCAAAGCCTAAATGTTCTGCTTTATTCTTCC  
TTATTATAATTCATAGGTAATATATTTTATGTTTGCAATGAATGCAGTG  
ATATTAGATCTCTAAGAGGTGCTAAAAATGAAAAGTACATATTTCAATTT  
TTCCCAATTTTCTTCTCTTCCATGAATGAAAAATATACATATTTGATG  
ATTTCCAAGTTTATACAACCGATCTTTCTCTTAGTTTTCTCTTACCAAAT  
TCCCTCCCTCACTCAGCCACCAGCCAGTCCAACCTGTGCTACCTGCACAGC  
AGCCCTCATACCATCCACACTCTCATCAGGATCCTGCCTGACCTGCGAGG  
AGCAGCAGCAAGAAGGAGACAGAACCTCCACGCTGAGCATCTCAGGGCTT  
TCTCAGAGACTCCAGAGACCCTGATAGGGACAGAGCCTGGCCAGCAATC  
CATGCTGCCAGCTGTATGATTGTGGGCATGTAAATCTCAACTGAAAATG  
GGTGTAAATAATAACATGTTCTTCCCAGAAATGAGCTTTATGAAGATCATAT  
AGCTGTTTTGAACTCAGACAAGCACTGGTAGGAATACAAACAGGGGAGCC  
AACAGCCTATAAATAATACTTTAAGAAAGGGCATGAATGTAATTACTTAG  
GAACAAAAGGCAAAGTGAGAGATGCCTAGGACTGAGCTGGACAAGCTGC  
ACCTTTTAGTGGCTCAGCCCATGGGCTGACAAGGAAAATGGAGGAGCTAC  
CAAAGAAGGTGGAAGGATTCTGGGAGAGTGGCCCTCACCTGCCCAGGGC  
AGGGCTCAGTGGGAGAGAGGGAGATCTGTTATAAATGCTGCCAGGAGGTC  
GAGTCATGTGAGAATGTCCATGTGAAAAACATCCACTGTGTGTATCTAAAG  
AGAGTGGCTGTAAAACAGGTGAGGGTCAAAGGTCTTATTGTCTCAGATGT  
TATCTGCATGCATTGTCTCAGCAACAGAAAATAAGGAGCATGGACACA  
AAGGGTTAGGTTGAAGCAAAAATTTAATAAGTGAAAGAAGAAGGCTCTCT  
GCAGTGGAGAGGGGAGTCTGAGTGGGTTGCCACTTTGACAGCTGAATCCA  
AAAGCTTTTATAAGAACTCTTCTCATATCTGCAGCTGTTTGAGTAACTT  
CTCTTACCTATAAAACTGTCTGTATAACTCTCCCTTATCTATGCAGCTGT  
GGGATGTCTCCAGGTAAGCATAAAGTGAGCTTCTCTGTTTGTATAACT  
GTGGGTTTGTGTTTAGGCAAGCCCCCATCCCTCCCTGTGTAAGCTCCCAT  
GGAGCCCACCATGTGCATATCTGAGAAGTGAGGAAGCTTTCTCTGGGAG  
CTCACTGATCGTACAAAGAACAAGAGGCTTCTGTGCCGCTTATCTATTCA  
GGTGCAGCCTGAGTTTTCCCAGGCTGCTCTATTTTGCCTGTAGCTATG  
ATTTTTCAGGCAGGCTGCTTCTCTGAAGACTAGCCTTAACTGTCTACCTA  
TCAGATTTTTCTTTTCTTCTCCCTCAGCTGGTTCCCTCACCAAGGCTG  
AGCAAGTGAAAAGGAGGGCACAGGGCAGGCCAGTAGTGAGCAGCAACAAG  
GAACCTAAGACAGCAGAAACCACTCTTACACCTGGGTTGAAAGGGGTGGG

FIG. 4 (31 of 61)

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GAGCCAGGACTACAGC1 AGGTAAGAACATAGGTAAAGAGATACTGTTGT  
TGTGTTGTTTTAACTATGAGAAGCATTGAGCTTTAAATTTCTACAGGAA  
GGATCCAGTTTCAGACAGGAGCACCAATATTCAGAAGAGAAGACATGGT  
GTAAAGGTCCTGGGAAGGCTGAGAGGATTGGGACTCAGAATCCAGAGCAG  
AAGCCGTCTGTGAACAGAAGAAGGACCTCCCCAGTGTAGCAAGAGGGAG  
GGAGGAGGGACAGATGCCAAGATGGTTCAGGAAGAAGGTTTGGTGGTAAA  
TGTGAGGCTGTGCTCACCTGCTGGCTTCAATTTCTCTTTAAATGTGAG  
ATGGAATCATTGATGAAGGCCATGCCATGCAATGAAATGGCAGTCTGAG  
GCATGGAGCAGCTCCAGCTTAGCCCGTGTAGGGTAATTATGGCTCAA  
CCCAGGAGATGAATATGACTAGGGAAGTGAAGTCCAAAAACAAATGGTC  
TCAAGTTGACTGTGAGTCTTCTGGGAGGCTGAGACGACAGGTGGGGTTGA  
CAAGGGAAGGGGAACCCACCTGCTGAAAAACATCAGGCTGTTGGCTGGG  
GAGGGGTGAGGCCTGTGTTGTAGAGATGGATGGATGCCTAAAGTTGGGTA  
AAGGTTTCAACTCTACCTCTGCTGGGTGTGAAATAAACAAAGACCACC  
CAAATGAGAACAAACAAAGACTATTTATCCAGAGCTTGCTCTGACAAGG  
AGTCGGCAACCATCACTTGCTTGGCAGAGACTCAGAAGTAAGCAGGGGAG  
AAAGCCTCATAGCAGAAAGAAGGGAAGTCTTCATGTATGCCCTGAGTGGC  
AGCTGTAGATGTGGGTGAGTTGCAGGTGGCTAACTAGAAATGGGGGACTC  
CTGTGTGATTGATTAGGAGCATGTTTGGCTTCTCTGGTTGGTCTACAT  
TGGAAGAGGGGAACAAAAATTTAGGGCAGTTGTCAGTTATTAATCAAGTG  
TTGGCCATTTTGTACTGACTGTTACAGGAGTGAAGTGGCTCCCTGGATTGT  
TTGCTAGAAATAGTGGTCTTCACTTCTGCAAGTCTGACTTTCTGGTAAT  
AGGCTTCTGGGTGGCTATTGTGGATAATAAGTGGGTTTCTGAGCTGA  
TTCTGAGATTGTGGATCAGAGTTATTTATATAAACAGTCTGACCATT  
TTCCACTGGCATATTCATCTTCCAAGAGCTGGCCAAGCTGCTGTCTTAT  
CTGTCTCCCCAGCCCCCTCACTCTGGCTGTGAAATACAAGCCACTAGG  
TGAGGAATGGGGACAATTGAAGACTGAAAGCTTTTCTTGGCTGGGTTCGC  
AGAGCTGAGGAAAGAAATGACAACATCCAAGTGTCTGCCCTGGGCCAGTT  
TTAGGACTGTAGTGGTAATGCAAGGACTGTGTGAGTTTATATTTTCAAT  
GTCTCTCTAACTAAGGTGGAAAAAAGAGGAAATGCTGTCTGCA  
GTCTCTGCAAAAGTCTAACTGTGCTTCCCAACATTGCAGCCATTAGCC  
ACAGGTGAGTATCAAGCACTTTAAATGAGACTGGTCCAACTGAGATGTG  
CTCTGAGATAAATACACAGCAGATTTCAAAGACCTAGTACATGCCCTG  
ATTTCAAGCTATATTACAAAGCTGTGGTAATCAAAACAGTATGGCATTGG  
GAAAAAATAGACACATTGGTCAATGTGACAGAATAGAGAGCCCAGAAAT  
AAACCCGTGCATGTATAGTCAACTAATCTTGACAAGAGTACCAAGAATA  
CACAATGGGGAAAGTCTCTTCAATAAGTGGTGTGGGAAACTAGATATC  
CACATGCAAAAGAAAGAAATTAGACCCTTGTATTACACAAATCTAAAT  
TAATTCAAAATAGAAAAAGACTTACATGTAAGATCTAAACCATAAACT  
CCTAGAAGAAACATAGGGAAAGAGCTCCTTGACACTGGCATTAGCAGTA  
ATTTTTCAGATATAACATCAAAAGTACAGGCAATGAAAGCAAAACAAGT  
GAGATATATCAAACTAAAAAGTTTCTGCACAGCATAAACATCAACAGA  
GTAAAGACATGACGTATGGAATGAGAGAAATATTGACATCTGACAAAGG  
GTTAATATCAAAATATATAAGTAATTCACACAACCTCAGTAACAAAAGCC  
AAATAACCTGACTTTTTTTTTTAAATGGGCAAGTACCTGAATAGGTATTC  
CTCAAAAGAGACATACAAATGGCCAAGAGATGTATGAAAGCTGCTTAA  
CATACTAATCATCAGAGAAATACACAAATCAAAACAAGATATCATCTCA  
CACCTGTTAGAATGGCTATTATTAAAAATGAGATAAGTGTGGCCAGGT  
GTGGAGGAAAGGAAACCCCTTGACATTATTATAGGAATGTAAATTAGTA  
CAGCCATTATGGAGAACAGTATGGAGATTCCCTAACAAATTTAAATAG  
AATTACCATATGACCCAGCAATTCCACTTCAAGGAATACATTCAAATACT  
ATCAGTATCTCAATAAGATACTTGCACTCCTATGTTCTGTCAGCGTTAT  
TCACCATAGCCAAGATACAGAAACAAGTTAAATGTCCATCAACAGATAAA  
TGGATAAAGAAATCAGGTACATATATATACAATGGAATATTATTAG  
CAAAATCCTGACATCTGAGATAACCTGGATAAACCTGGAGGACATTATGC  
TAAGTAAATCAAAGCCTGACACAGAAAGACAAATACCACATAATCTCAC  
TTACATATGAAATATGAAATGTTAATTTTATGGAACAGAGTAGAATGG  
TAGTTGCCAGAGCCTGAGAGTAGAGAAATGAGATGCTTGTCAAATCAA  
TCATCACATTGAATATATATAATCTATTTGTCAATTAATATTTTAAGAA  
TAAAAAATACCTGGCACCAAAAAAAGAAATGCAAAATGTCTCAACAATGTT

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ATATGTATTGCATTTTG. AGTGATAATAATTTGAATATTAGGTTAAATAA  
AATATATTTGAAAAATTAACCTCACCTATTTCTTTCCATTTTGTTAACA  
TAGGTACAAAAAAATTAATAATTACCTATGTGGCTCATGTAGGTGGCTC  
ACATTATACTTTGATGACACTATACAGGCTGGTGACCATATATCTCTTAG  
ACTAGTCTAAGTGATTTAACAGTGGTTCCAGAAAGATCCAGGTTTAACAC  
CAATGAAAGGGCCAGCTGGCTTAGCCCAGCTTGTGTGGGAAATGTTGGGG  
AGTGGTTTAAGACAGGGAAAGCAAACTTTTGATGCTATTGACTTTTGTG  
AAAAATCTTTTGTGGCTGAAAAAACCAAAACATTATT  
>Contig49  
GCTCGAGTGTGTCTCTAAAGCCTTTCCCCCATTGGGCTCCACTATACGCAC  
TCTCCTGGTTTCTCCTCCCTCTAGCCGCTGTCTTTGGTCTCCTTTCTGATT  
TTGCTGCGTCTCTGTCCCTGAATGATTGCTTCTCCACTACGGGGTGAT  
TTTGCTCCCCAGGGGACATTTGGCAATATCTGGAGAGGTCTATGTTGTG  
TTTGAGGGTGTGTCTACTGCCATCTAGTGGGGAGAGGCTAAAGATGCTGT  
TAATGCCCAGGACAGTCCCCATAACACAGAATTATTCAGCTCAAAATATC  
CATGGTGCCAAGATCAAGAAACCTGCTCAAAATTTAGCATGCTGCTGAAG  
GCCCTTCTCTTTCTTTAGCAATATCTGCCTCCTTAGGGATCTTTTCTAG  
TCTCAGTGGTTTAAACATTTAAATCCCAAATTAGGCAATAAATTGGGCCC  
CAAACCTCGTTAGTATATAAAATGTAGAACTGTGTTATTAGAAGGCTAATAA  
AATGACCTGGTGAGCATCTGCAGCTAGCCTCTGAGCAATTCTGGGGACCA  
CGTGCAAGATAAATCCATCTGTTCCCTCTCTGTAATGTGGCGCTACCTTG  
TGGCCGATTTTTCTCGGGTTAAATATCTCTGGGGATGCAACTTGTCTGTG  
GTTAATGGCTGTGTGAGGCCAGCGCTGGTGATAAAGGAATCAATCAAGA  
CAATATTGAATTTAGAAAGGCAGATTTATTTAGAGAAAAGGAGAGATACG  
TTGCAAGGGAGCAATGGGCAATACAGCAGAGGGAAGGCTGTCTGCAAGA  
GGCAAGGGCTACGTATGACGTAGGGCTGCTTAGGCTGAATGCTTGCAGAC  
AAGATGCTTGCCTGCAGGTGGGCTGTGAGCTGAGTCTTGGGTGCTAGTG  
AGCCATTGGCAGCTGACCTATTTCTTGGAACATTGCTCCCTGCAAGCA  
TTTTAATGTTAAACCGCCAGGTCAGTTTGAATTTCTTTTTTCTTTTTT  
TTTTTTTTTTTTTGCTTTAGTAGGACCTGCCGTTGTGAGACTATCTGAGG  
TAAATTAGACACCTCCTGGTTTAAAGTACCCGCTCCAGTGACTAGGCAGG  
GAGCTCTTCTTGAAGAGGGTGTGGGCAGTGGGTACTTTGCATGTTGTCC  
ACACCAGGCGAGCTGCTGCTTCAGGGCCTTTGCATTTGCTCTTTCTTTG  
CCCAAATGCACTTCTCTCACTGTTTACATGATTTTCTCCCTCTTTTCC  
TTTTAGTCTTTGCTTAAATATCACCTTCTAGGGAGGCCTTCCACACCAC  
CTCTTCAAGATTTGAGGGTATGCACCCCCACCCCTAGCCTTCTTATCCCT  
CTCCACTGCTTTCTTCTCAAAGCACTTGTTACGTTCAAATAAAATAGATT  
AGTTACTTTATAGTTCTAATTTTACTATTTTGTGTTACTTCAATAC  
CCATGTAATCTCTGGAAGGAACGTTTCTTTTGTAGTGTATTTCTAGCAC  
CTAGAACAGTACTTGGCACATGGCAGGTGTTCAAAGTATTTGTTGATTA  
TTTTCTCAAAGGGCATGGAGTCTTAGAAGTTTGAGAACACAGTTCTAAGC  
ACAGCTGTTTAGAGACTATGGATGATGCTAATGGCTGTATTCCCAGTAGG  
TGGGGCAATTCTCAAATTGACCTGGAATCCTTGAGATCTGGGGACAGTCA  
CCAAGCACTGGGCTCTGTGGGGAGAGATGTGCTGGTTTTTAGAGAGGAGA  
ATAGCATCCTGGGGGACTTGGCCCCAGGGCTTTCTGTCCCAATCTCTTC  
CCAAGTGAATCCAGAGGCAGGAGGCTTGTCTGTAGCTGGTCAGTCTGT  
TAAGTGTTCCTCCCATCTACACAGATGCAAGAAGGCTGAGAAAAGCA  
AGCTGTGAGGTGAGCAGGGGCCCTGACTCCTCCCCAGAAGGCACTCAGAA  
CTTCCATAGGGCAACTGGAAGAAGGTTCTACTTCTCACCAGGAGCTGT  
TGCTGGGGAAAAAACAGCCTCAGGCCCTACCCTGTGCTGAGAACCTGAA  
TCCAGTATCAGGTTCTCCAACAACTTGGATCCAGCTGACCCTCACAAGG  
GGTCAGATGCAACCTTGTAGCATATGGAATGGCAGCAAGGTCCTTGTG  
TGGACTATGCTTGAATCTAAATTAAGACAAGGCCTCAGAGGGGCTAAGT  
GACATCTGTCTCCAAAGTTTACAGCTAGTGTGACTAAATCTTGATTC  
CACCCTCTCAGGTTTTACCATAATCCAAAAAAGGTTGAAAACAAGAAAAG  
TTATCTTTGGGCAATTACCTCTTTCTGTTTCTTGTCTTACCTACTAATGT  
TCTAGGCTCACCCTCTGGTCTGCAATCTCACTGAAGTACAGATCCCTCA  
TGGCCTAAAGGGTTTTACACTGGGTTGACTAGGCTCTCCATTGCCTGT  
CCTACTGTCTAAGGCACCTCCTGGGTAGGTTGCCAGCGTCATTCTGATG  
CTGCCGACTTTCTTCCAGCTACTTTTGAACTTGGTATCCATGGCAGA

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FIG. 4 (34 of 61



TCCCAGCGTGATTTGGC .TACTTTGGGAGGCTGAAGCGGGTGGATTG .  
TGAGCTCAGGAATTCAAGACCAGCCTGGTCAACACGGTGAAACCTATCT  
CTACTAAAAATACAAAAAATTAGCCGGGCATGGTGGCAGGCGCCTATAATC  
CCAGCTACTTTGGGAGGCTGAGGCAGGAGAATCGCTTGAACCCAGGAGGCG  
GATGTTGTCATGAGCTGAGATCGCGCCATTGCACTCAAGCCAGGGCAAGA  
ATAACAAGACTCTGTCTCACAACAAACAAGCGAACATACGAAACAAACGT  
AACATCCAAACTAGCAGGTACATGCCGTGCCAGTCATGACCCATGGTCAT  
AAGATGTCTACAGCTCAGGAAGCAGCTGCACAATGCCTGCATAGACAAAC  
TCTTATGAAAGCAGAATGTCTGTATGTCTCCATAACACATAACAGTGTAT  
GCTTTTATTATGGTCTACTCTAGCTGTGTATGTACCTACGCTCTAATATG  
CCAACGATAGTTTTCTTTAAATCATCAACATAATAAATGTATGCTGTCA  
GTCCCCCACATGTAGACATAACTTAGCTGGTACATGGATAAGAAACCTAT  
ATTAGATAACCTTAGGCCAGGTGTGGTGGCTCATGCCTGTAATCCCAGCA  
CTTTGGGGAGGCCGAAGCGGGTGGATCACGAGGTCAGGAGATCGAGACCA  
CCCTGGGCTAACACAGTGAAACCCCGTCTCTACTAAAAATACAAAAA  
TTAACCGGGCATGGTGGCAGGCACCTGTGGTCCCAGCTACTCAGGAAGCT  
GAGGCGGGAGAATGGCGTGAACCCAGGAGGCGGAGGTTGCAGTAAGCCGA  
GATCACACACTGCACCTCCAGCCTGGGGACAGAGCGCAAGATTTTCGTCT  
CCCAACCCCAAAAANCNNNNNAATTTGCACCCAAATCTGACTAATTCCA  
GAGCCAATTTCAAATTTAGAATCGTTATATCTCCCTGGTGAAGCTT  
TTATCTTTAAGGAGACACACTCTTTATGTCTACCAATGCTTATTGECTTA  
AAGTCCACTTTGTGAGATACAGCTGCTTTCTTTAATTAGTTTTTGTGTG  
GTATATCTCTTTCCATCCTTTTTCTTTTCTTTTCTTTTCTTTTCTTTT  
TAGATATATTTCTTTTTCTTTTTTTTTTGGAGAGAGAGTCTCACTCTCTC  
GCCAGGCTGGAGTAGTGCAATGGCGGATCTTAGCTCACTGCAACCTCC  
ACCTCGTGGTTCAAGCAATTTCTCTGCTCAGCCTCCCAAGTAGCTGGG  
ATTACAGGAGCCACACCAAGCCAGCTAATTTGTTGTATTTTTAGAAAG  
AGATGAGGTTTCGCCATGTTGGCCAGGCTGGTCTCGAACTCCTGACCTCA  
GGTCATCCACCCACCTCGGCTTTCCCAAAGTGTGGTATTACAGGCGCGA  
GCCACCATGCCAGCTGATTTTAGCTGTATCTCAAAAACAGCATGGGTTC  
TGTTTGCTTTCTTTATTAGCTTTTATAATGTAAATCATTTACATCAAACA  
TCTAATACACCATGGACTGTAAACACAGCCATATTTTATGTATGAATTA  
AAAAAATAACACCAACCAATTTAGTTCTCTGAGACACACACCTTAACAATAT  
CTCTGTGATGTGCATAAATCAATCACATCAGTTTCTCTGCACCTCAAAAT  
TTCTTTCTCAATTTCTCAGAGATATGGCAATTTCTCTGGTTTTACATTCC  
CAGAAGCAAAGAAAAAGTACACAGCTTCTTCAAGTCATGAGTAGCTTCTT  
TTTTATAGCTCTTGGTGTGTTGCAAAAAGATTGGAATTGCTTCACTAATA  
CTAAATTTTCAATCTGCTGCTCTGTTTCTATGACAAGTCAGAGGGCATCT  
TTTTGAAGACATTCTAAACAGCAATTAACCTCAAAACATGTAATGACAAT  
GACACACAAAACCTCAACTGATGACCAATGAAGAGTTCCAGCCAAAGTTGA  
CACAAGCTGGCTGACAGAGCTTGTAATACACACAGCTTGGCATATGCCTC  
GCCATTTAGAGATGTAAAAATAGGAATAAATGTTTTCCCTTAAATCAAT  
GAAATAGAGCATTGAGTGAATAATCTACGACAGTTATAGTGTCTTCTAT  
TCATTATTCTCATTCTGTTTCTTCTCCCCCTTGTCTTTTAGTTTGAA  
TATTTTCTATCATTTCATTTTCTTCTCTACTAGTTTGAACTTATGCATT  
TATTTTCTATTTTATGACTTACCTAAAATTACTCTGTAATCCATGGAT  
CCTTAATTTATTTAAAAAATAATGTTAATGAGTAGCTTTATTTTCTTCC  
CATCTAATTTAAGGCCACAGAACACCTTCACTTACCTCAATCCTCTCCC  
AACTTACATGCTTTTAAATGTATATATGTTAATACCGTATACTTTTAAAA  
CTTTCTAAATAGCATTATTTTATAGCATGAGTGTTCATTTACATTTTGT  
CATATATTTAGAATTTTCTTTGCTCTTCTGTTTCTTCTTCTATTTATGACT  
CCCCCTCTGGGATCATTTTCTTCTACTTGAAGTACATAGTTTGAAGTGC  
ACTATTCAATACAGTAGCCACTAGCCATGTGTAGCTATTGAAGTTTAAAC  
TAAGTAAATTTAGTAATATTTAAAAAATCAGTTCTTCTCATCTCACTAGCC  
ACATTTCAAGTGCTCAGCAGCCACATGTGACTAATGACTACTGTACAGCA  
AACATATAGAACATTTCCATCATGGCAAAGAGCTCTATTGATAGTGTTC  
TCCAGAGTTTTCTGTTCCAGGACCAAACTGAGGGTTGGGCTGCTATTTCTC  
ATGGCCCAATAACAAGATGCAGATGAGCTGGGGAGGAAGAGAGTTTTTAT  
TTCTGCAACCAGTTACAGGGAGAAGGCTGGAAATCATCACCAGGCCAAC  
TCAAAATTATGACGTTTTCCAGAGCTTATATACCTTCTAAGCTATATGTC

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TACGTGTAAGTGTGCAT1 JACCTGAAGACGTAAGTGATTAACCTCTTTT  
ATCTGTAACCTAAGGTCTGAGTCCGGAAGATCTTCCCCTGGAGCCTCAGTA  
AATTTACTTAATCTAAATGGGTCCAGGTGCTGGGGTAATTACCTTATCT  
TGTCCCCTGTCTAAATCATGGAGGTTTGGGGAATTCCTTTAGAGCACCAT  
TAACCTGTTTGTGTAAGGCCTGGGAATTTCTCCAAACCCCATTAACC  
TGTTTAATCCCAAATTTGGTTCCGTTAAAAATTCCTCCTTAATTTGTCCA  
ATTTTAAAGGCCCAAAAAAGGCTGGGGCAAACCTCTGAATGGCCTTTGTT  
ACATTCACACCTTTGTTTAAAAACACCGGTTTTTAATATTTAACTTAACC  
ATTTAATCTCTACTGAAACACTTGTATATAAATCTGCATTAATGAGAAC  
TGGCCTGCGCCATATCTCCTTCTCAGAATATCTTAGGGTTGTGATCCCCCT  
GTGTGAAGAGAATATATCTCTGGAGATCTCAATCTCTCTACCCCAAAAAA  
AATCTCACTCGGAGAAAACCTCAGACTCTTATCTCCACAGCGCTATCTCTC  
TCCTCTCC  
>Contig50  
GCTTGTCTAAGATGGTGTCTCCTTGTGCTGTGCCTGCTTTCATCCTGGGA  
TCTCCCTTCACCATCAGGATTGCCTTCACCTCATTCCAGTCTTGGATCTT  
TCTTCTTGTTCCTTGAGTATTTTTTTTTTTTTTTTGTGCTGCAATCCCTTCA  
GTGGCCTCTTGGGAAAAGATGTGTAGGGAGAAAAATTTCTTTAGAAACT  
TGCATATCTGACAATATATTTATCCTATCCTGACATTTGGTAGATAGTTC  
AGCTGGGTACAGAATCTAATTAATTTTCTTCTGATTTATAAGACATT  
GCTCCATTTTCTTCTGGCTTCCAATATTGCTGCTGAGAAGTCTGACACCA  
TTCAAATGCCTGATTTTTTCCATGTGATTGTTGTTTTCTGTCTGGAGTGT  
TGTAGGATTGCCTCTTTATCTACAGTGTCTGAAATTTTCATGACGTAGGT  
CTTCTTTCATTCTATTATGGTAGACACTCAGTGGGCCATTTAATCGGGAAA  
AACATGTGTTCTTCAAGTTCTACAACTTTATTACTTCTTTTTCTTGTG  
TCTTCTCTGGTCTGTTTTTCAAGCCCGAGTCTCTTAGATCTGTCTCTCTAA  
TATTCCTATTGACTTTACTTCAATTTCTAAGTCTTTATCCTTTTGCTTTA  
CTTTCCGAGAGACCTGCTTAACCTTATCTCCAACTCTTTTATTGAATTT  
CATTTCTTTTACTATATATTTTTTACTTTGAATACACCTCTCTCTCTCTC  
ACATTTTCCCCCATAGTATTTTGTCTTCAATTGACAGTCTACTATCTTA  
TTACTCTGGAGATATTAATAATAGTTTTTAAATTTTATTTATTTTTATT  
TTCAAACAGTGTCTTACTCTGTCACTCAGGCTGGAGTGCAGTGGTGTGA  
TCATGGATCACTGCAGCCTTGATCTCTGAGCTCAAGCTATCCTCCTGCTT  
CAGCCTCCCAAGTAGCTGGAACCAAGGCATGTGTCAACATACCCAGCTA  
ATTTTTTTGTTTTTGGGTGGAGTCTCACTCTGTAGCCCGGTCTGGAGTG  
CAGTGGTGAATCTGGGCTCACAGCAACCTCTGCCTCCTGGGTCTGGTT  
CAAGCAATTCTCCTGCCTCAGCCTCCTGAGTAGCTGGGATTACAGAAACA  
CACTACCATGCCCAGCTAATTTTTGTATTTTTGTAGAGACAGGTTTCACC  
ATGTTGGGCAGCCTGGGTCTGAACCTCTGACTTGTGATCTGCCCACTTGG  
GCTCCCCAAAGTGTGGGATTACAGGCGTGAGCCACTGCACCCGGCCACT  
AATTTTTAAATTTGTTAATAAAGACGAGGTCTTGCTATGTTGCCAGTATG  
GTCTTGAACCTCGTGGGCTTAAGTAATCTTCTGCCTCAGCCTCCCAAAGTG  
TTGGGATTACAGGTGTGAGCCACTGAATCTGACATTTTTTAAAAAGTTTTT  
TTCTCTTTACCAAGTCTTTTTTCCCTTTCTGCTTTTTTGGGTGTTTTTA  
TTTTGATCTCTATCTTGCTAGAACTTTCTGGAGACGTTTAGTAATACTA  
GATTTTTGAGAGTGGGCAACTGGAAAGCTGATTGGAACTCTGAATACAT  
GGGTGAGGCTTGTGGCTGTGAGTGTCAATGCTTGATGTCTGGCAAGGC  
CAATGGGTTTGGGACCCCTACTATTAGTATAGGCTGATTCCCTGGGAAA  
GGCTCTTTTGATCTCCTGCCTGGAGGATAAAGGCCTGGCTACCAGCCTTC  
TGTGTGTAATGTGAGGGAGAAGGCTGGAGTATTCAACATCATGCTGAAT  
CCTTTCAATGATCATCTTGTTTTTTAGTAATCTCCTACCTTAACCTCTGT  
CTTCTGCTAGTATGGGAAAGATGACCTGAAAATCTAACCATTATTTTTTC  
CCCCATTAATATCATTTTATGATTATTCAGAAGTTAAATAATTGTCATGC  
TGTCCTCCAAAAGACTGAATCAACTAGCAACAAATAAGAATTTCTCAC  
AGCTCTGCCAGCATTTTAAAAGAATAGCTTTATTGAGCCCAGGAGGTCAA  
GGCTGCAGTGAGCTGTGATTACACCACTCTACCCAGCCTGGGTGACAGA  
GCAAACCCCTGTCTCAAAAAAGAAATTTAAGGAACAGCTTTATTGTTGTA  
AAATAGACATACAATAAACAGAGCACATTTAAATTGTGCAACTTATAC  
TTTGATATAACCCCTGTGAAAACATCACCACAATCAAGATAGTGAATATAT  
TTATCACCTCCTGATACAGTTTAGCTCTGTGTCCCCACCTAAGTCTCATG

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TTGAATTGTAATCCCCAATGCTGGGGGAGGGGCTTTGTGGGAGGTGAT1G  
AATTGTGGGGGTGCACTTCCCCCTTGCTGTTCTTGAGATAGTGAATGAGC  
TCTCATGAGCTCCCCCTTCACTCACTCTCTTTCTGCTGCCATGTGAGGAT  
GTGCTTGCCCTCTTCTTTGCCCTTCTGCCAIGATGTGTTTCTGAGTCCTC  
CCTAACCATGCTCCTGTACAGCTTGCAGAACTGTGAGTCAGTTAAATCT  
CTTTTCTTCATAAAATTACCCAGTCTCAGGTGGCTCTTTATAGCAGTGTGA  
AAAGGAACTAATATACCTCCTAAGTTACCTCAAGCTTCTTCTTAATTCCT  
TCTCCTCCCTTCTTCAATTGCCAAGCAAACAACCACCTGTTTTCTGTAC  
TATAGATTAGTTTACATTTTGTGGGTTTTTTTTTTTTTTTGTAGACAAGGTC  
TCACTCTGTTGCCAGGATGGAGTGCAGTGGTGGCATCATAGCTCATTGC  
AGCCTTGAACCTCTAGTTTCAAGTGGTCCCTCCCACTTCAGCCTCCTGAGT  
ACCTGGGACTACAGGGGTACACCACCACAACTGGCTTAAAAAATTTTTTA  
AATAAAAATGGGGTCTTGTTATGTTTCTCAGGCTGGTCTCGAACTCCTCG  
CCTCAAGCAGCCCTCCCTCCTTGGCCTCCCAAATTGTTGGGATTACAGGC  
ATGAGTCATGACTCCTGGCCTAGTTTACATTTTCTAGAGTTTGTATAAA  
TGGAAACATACAGAATGTATTTTTTGCAGGAGTGGGGGAGTGTCTATT  
TCTTTCTTTCTTTTTCTTTTTTTTTTTTTTTTTTTTGTAGACGGAGTCTCG  
CTCTGTCTGTTGCCAGGCTGGAGTGCAGTGGTGGCATCTCGGCTCACCG  
CAAGCTCCACCTCCCGGGTTCAAGCAATTCTCCTGCCTCAGCCTCCTGAG  
TAGCTGGGACTACAGGCGCCGCCACCACTGGCTAATTTTTTTTGT  
TTTTTGGTAGAGACGGGGTTTTCCCATGTTAGCCAGGATGGTCTCGATCT  
CCTGACCTCGTGATCTGCCCGCTTCGGCCTCCCTAAGTGCTGGGATTACA  
GGCGTGAGCCACCGTGCCCGGCCCAAGTGTCTATTCTTAAACCAGCTT  
TCATGCAATCTTTTTTATTTTACCATCTCTGTGATCCCACTCCCAAAGG  
TACTAGATGTCGATTGGTCTTAGGATCAGCTACCATTTGCCAACTGCT  
TTCCAGCCTTCCAAAAATTTTTTCTTTTTTCTTAAAGATACTCCTGTG  
TGAGGCTCAGAACTCTGAATTGCTACTGCAATATGAACTCGGTGATGT  
GAATGCCAGGGAATTGCCTGATTGATCAAAGAAATGTATCCCTTCTCCC  
TCACTCTTGCTGTCTTCTCATTTGTTTTCCCCATCCTTGTTGGATTCTGTA  
ATTTAAATATCCCTTTAATGTTATAATATTTAATGGCGTTTGGCGAAAA  
GTACAGAATTAGGTGCAAGAGTGCATAGCTGTTATTTTTTTTTTGGCCTC  
TGAGACTGTTTATATATGCAAGTTATTTAACAGAAAGTTCTGCAGTGACC  
TGAGATGTCAGGGGGTCTGATAGAGTACGTTTGAAGGCAGTTACTGGAA  
AAAAATAATGCCATTTCTGGTTTGTACTTCGGTAAGTTTCAATGACCCAA  
TATATTGTTTACATGTGGCATTTCAGTAAAAAGTAGCTTCCCTCCCTTT  
CTTCTTCTTTTTCTCTTTCTGCTTCTATAAAGCATCTGCTTTGGGAAA  
CTTCTTAGGAGGAGAGCTTGCCAGCCCGTGGGTAATGGAGAGGTCTTGCA  
GAGATAAAGAGATGCTCCCACTCAATGCAGGATGGTGTGGAGGTAAATG  
GGGATACGTCTGGCATCACTCAGGAATGGGCCTTCTGGCAGGGAAGAGA  
AGGGAGGGGAAAGAGGAAGGGAGTCAAAGATGAATTGCTGAATACGGGGA  
TTCCAGGGCCTGGAGCCAGGAAGAGAACTTTGGGAGGTGTGAACCTGGAG  
GGCATCAGCTGATGAGGAGCAGCCTGAAGTCCGGGGAGGACCTGTTTTG  
GTGGCCAGGAAGAAAGTGCCTTCCACACACAGGGAGGCCACAAGGCTGAT  
GGGCTGGGGGTTGGAAGGACAGCCCTAGGACAGGCTTGGGAAGCAGGCTC  
AGGTAGGGACTGCGAGGTTCTTGTTGAGTCTTTTTCATTCCTGGTCTTAG  
AAAAATAGAATCCAAGGCCTCTTGAGAGTGAAGGTGGGTTGGGAGGAGGG  
CAGATGGGGCTTAGGCCCAGGACACCCGTAGAGCTACTGCCAGCTGTCT  
CTCAGGGACTCTGCTGAGGTCACTCCAAGGATCATTCCTAGCCTTGCTAG  
ACAGTACTGACAGAGGGAAACCGTAGTATCGCACCCACTTCTTCTCTTTC  
AATGAAAGTTTAAAGGTCACCATTTCTCTGGCAAAGGAAGTTCCACAAA  
TATTCCATTTCCGGTCTTAGAAACAGCAAGGTATCAAGCAATTGCAAACT  
TCCTGTGCTGGGGAATTTCCCAAGGAAGTAGGGGCAGAGTTCTGGTGGAGA  
CAAAGTGAATTCCGAGTGATTAGTCAGTAGCAGTAGCAGTAGCAGTAGCA  
GTAGCAGTAGCAGTAGCAGTAGCAGTAGCAGTAGCAGTAGCAGTAGCAGC  
AGCAGAACCAAGAAATTTCCCGCACGTGTCTCAGGCTCTCATTTGCCAACT  
CAGTCTCTAAGTATTTTTTATTTGGCAGGAAAAATAAAATAGCTATGAGTGA  
AATAATTCAATAGACCTGAGCCTCCATCAATTTTGTGTTTAAAGGCCTGA  
CTCTCTTACCTTTCCCTGGGATGGAAGATGCAATGTTCTGATGTAC  
TGTCAAAAAAGAAGAACAGTGGGTATATTGTATGCTTGAGTTCCAGCCA  
TTTGTACAAATAGATAGAGATGACTGCCATGTGTGTAGACTTTCTATAGA

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CTGTGTGCTAAACCCGACTGCCACTTCCAAGGAGTAGATGAGGAATG.C  
CATGGTTCTGGGGAGCCCTACCCCAATTTGGGGCAGACATTCCAAAGCTC  
ATTTTCTGTGGAGGGGGTTGATGGTTAAAGGACGGCCTGGGAGTAACTCG  
TCTGTACTAGGGCCAGGAGAGTTACATGCTGCTTCCCATGTTATTCTATC  
ATTCCCCCATGTGAATAGCTATGGCGTGAGGTCCAAGGTTAGGGCCTTTC  
TACCATAAATGGGGGAATAAAATCCCCTACCAGCCTGAGAAGTTTCTGT  
TATAAAGAGGCTTTTTTTTTTGGGGGGTGGGGGAGCAAGCCGACTAATGT  
GTTATTTCCATACGGTTTGTGTTTTAAATGTAGATGTCATATGCAGGAGAG  
GTGGTGTAGTGAGTCAACGGGATTAGAAGGACCAGTCCGAAAAGCAGA  
AGAGGGTCAAGTTCAGGGCACTGAGGACTACTGCATTCACTGGCGTGAAA  
GGCAGATGGCTGAACAGGAGGGGGACATTACATTGCTTGTCTCCTTGAG  
CCTCGATTTCTCATCTAAAAAGAGGGTCATTTATTACAGAACATTTAT  
TAAACTTGTGCCAGGCACCGTGCCAGGAGCTGGACTAAAAATTAAATCCA  
CCCCTGTGAGCTGCTCTGAAGGCTAAAAATATGAAGTATGTAAAGTAACC  
AAGTGCTGTACACATGCAGCTATTCAATGACTGTGTGGGCATTGCGGCAG  
ATTTTAAATTTCTTTTTTATTCTTTCTTTTAGTGAGAGGTTGGTTG  
TTATTATTGTGCTGCTGTAAGTGTCTATTTCACTTGCTTTTTTGTGTC  
TCCAGCCCATTCCAGGGCTGTCTAAGACACTTCTTATCACCTAAATA  
ACCGGGGAGGCAAGCGCTTCTTAAGAGATGGATCCAGAAGAACATGC  
TGGTTTTCTGTAGAAAAAGGGGCTGTGGGAAGTAGAGATAAGAAGGGAAT  
TGGCCAAGATGAATGTACAGAGCCTTATTTTTTTTTTATAACACAGCAAG  
ATTAGATACAAAACAGGACAATAGCATCATCTGTTTTTATACTGGAAAG  
GACCTCACTTTACAGGTGGGAAGAAATAGAGTGGAGAAGTGAAGAGAATG  
GTCACAGAGTCAATCAGCATGTCTGCGTCAAAGCTGGGATTTCCCAATTCA  
GGGCTCTTACTACAGTGACGTATGGCTAATATTTTGGCATTGTTTCGGGG  
AAAAGCTGAAGCCCTGATGGTGTACGTCACTCTTGAGATAGTCTGTAGTC  
CAGCAGGGAGGAAAGCAAGGAAGGGAGGTGGAGGCAGCATTTTTGGGTGT  
AACATTTCTGTTCTTGTGTTTTGTGGCCAAATCATAGTGTGATTGGGACAAGC  
CACTGCCTTTCTCTGAGCCTCCACTTTCTTTTTCTTCTTAAGAGGGAGGG  
AATAGTAGAGTAAAGTAGTCACTTTTATCAAACACCTGCTATTTTGGAGC  
CATATTGCAAGTGGGTTGGGGGTTGAACACTTGGCTTTATTACCATAGG  
ATTAAATCCAACCTCGATACTGTGGCATTCCCAAACCTCCAGTCTAATCTT  
CTTCTCCATCAGCCATGCCCCACGACACCCTGGTCATATCTGATGTTGCC  
CCTTGCACTTGCCCCCTCCTTATCTTTGCTTTCTGACCTACCATATGGCT  
ATTGGTTGAAATTTCTATTTTCCAGGGCCTTGCTTAAATATCATCTCATC  
CATTAAACTTTCTTGAACCTCCCCTTGCCCTGTTCTCCCTAATGTCTC  
AAGCCAGAATTTATTTCTTTTGTGGCCAAGGGACTGGGTTTGTGACCTC  
TCTCAGGAGACTTAATATTGAGACCAAACGTCTTTAGACCTCACCAGCCA  
GAGAGATGAGCATCTATGGAATGCAGGCTTTTGCTGGACTTGCTGATGC  
AGGGCCTCTGCCTTCTCCAGGGCCTCTCCTGCTGTTTTAGGAATTTCCC  
TCATGGCACAGTCCATGAGCTCAGGGTCAAGTTCATACATGTTTTACTT  
CTTCTACTCTGCAATGGTCTTCTTGAACCTCTGAGGGTCTTAAAGCTGCT  
CTGCAGTTTTGTGGGGTGAGTAGAAAGGGGCTTTCAAAGTTGTGCTGTTG  
TTTCCCACCCCAATAGCATGAAACACAAAGATGCTTACAAATAGCTGCCT  
TGCTTTCTAGTCCCACTTCTCTCTCCTGAGGCTTTAAAACAAGTCCCCCT  
AGGTTGAGCTGGACTGGAGTTGTATCCTATCTTCATTATCTGTCTACTCT  
CTTTCTGCTCTCTAGAGAAGATATTATATATGTGTGTATGTATGTGTA  
TATATAATATCCATATATAGAACATATATTGTTATATTTACATATACATA  
CATAACATATGCATGTATTATATATACATATGTAGTATCAAAGTTGGAA  
TTAAACTGTATATTTTGTAAATTTGCTTTTATTTGCATCTATCACTGTAAA  
ATGAATATTTATCCATACCGTAAGATATTCTTCAATGTATTTTTTTTTTT  
TTTGAACAGGGTCTTGCTTTGTTGCCAGGCTGGAGTGCAATGACCCGA  
TCTTGGGTCACTGAGCCTTGACCTCCCCGGCTCAAGTGATCTTCCCACC  
TTAGCCCTCTGAGTAGCTGGGACTAAAGGTGTGTGCTCCACACCCAGCT  
TTTTAATTTTTTTGTATTTTTTTTTTAAAGACAGGGTTTTGCCACATTG  
CCCAAGCTGGTCTTGAGCTCCTGGGTCCAAGCAATCCTCCCACTTTGGCC  
TCCCAAAGTGCTAAGATTACAAGCATGAGCCACCACACCTGGCCTCAATG  
TAATTTTTAATGGCTGTATAGTATTCATCATGTGGTTGTACCCAAAATT  
ATTTAACAGTCCCCAGTTTATTTCAATTTTTTTTACTATTTGAATAA  
TGTTTTAGTAAATACCCACAAAATATGTACAATGGCTGGGCTTAGTGGCT

FIG. 4 (38 of 61)

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CACCCCTGTAATCCCAAACCTTTGGGAGTCTGAGGCAGGTGGGTCACTG  
AGGTGAGGAGTTGAGACCATCTTGGTTAACATGGTGAAACCCCGTCTCT  
ACCAAAAATACAAAAATTAGCCGGGTGTGGTGGCACACCTGTAATCGC  
AGCTACTTGGGAGGCTGAAGTAGGAAATCACTTGAACCTAGGAGGCGGA  
GGTTGCAGTGAGCCGAGATCACACTACTGTACTCCAGCATGGGCAACAGT  
GAGACTCCATCTCAAAAAAAAAAAAAAAAAAAAAAGTACAATTTGTTG  
TACCTCCCTGATTATTTCTTTTAAGTAGAATTTCTTATAATTTTTTTTA  
TAAGTAAAATTTGAATCAAGGGAGAAGCACCTGGAGTCCTTCAGATACC  
TATTGCCAAACTGAACTTTCTGTTCAGGTTTACTACATTCAGCCTGAC  
TCAGGGTTTGGGGAGTAGAGGAGGGGTGGAGGCAGAGGGCCTCTCCCTG  
TCCCCACAGACCTCCCTTGGTGAGGTCCAAGTCTGGACAGGTGGAGTGTG  
GCATTGCACCGTCAGGTCTCTGCTTCTGTAATTCCTTAAATCCATCCAG  
TGGAGCCTCATTGTTCAAGTCTTTTTTTTTTTTTTTTTTTTTTAACTCCC  
CTGAAGACGGAGTCTCACTCTGTGCGCCAGGCTGGAGTGCAGTGGCACGA  
TCTTGACTCATTTCACCTCTGCCTCCAGGTTCAAGTAATTCCTGCTGCC  
TCAGCCTCCTGAGTAGCTGGCACTACAGGCGTGATCATCACGCCCCGGCT  
AATTTTTTTTTTGTATTTTTTAGTAGAGACGGGTTTCCCATGTTGGCCAG  
GCTGGTCTCGAACTCCTAACCTTGTGATCTACCCGCTCTGCCTCCCAA  
GTGCTGGGCTTACAGGTGTGAGCCACCAGGCTGGCCTCAAGTCTATTTT  
TTAACTCCAGGAGGCTGGTATTCAGAGGGATTAGGGCTGGCAGAAGGGC  
CTCAAAGCTTTCAGGCTGGGGAATAGGCTGCAGCCTGGTTCAGGGTAA  
CCCAAGTGATTTTGGTTCCAAAGGGACAGGAAAAAAGTGATTGATATGG  
AAGTTGTCAAAGTGCAACTGTCAAGACATTAAAAAATGTAACCTTTTAC  
TAATATACAGTAGACTTGTGTTAAATATTTAACTGATTGTAAAAGGAAAA  
AACCAGACGCAGTTTTCCCTACCATACTGTCAACACCTCAACACTGAG  
TTCTTCTGTGACCTCTAGTCACCGAAATGCTTGGGGATTTCTCCACCAC  
TAGTCCTCCAGCAGCCGACACCAGTTGGGTGTCTAATTCCTCCAACAC  
TATCTACCTGGAGTTAGCGTTAGATCCACAGGTTGAGGGCTCAGTCTCA  
CAAGACTGCCTCCCACTTCAGGTGCCAGTTACAAGTGGTAGGTTGTCAAC  
TATGCTTCTGACTGATGGCTATAAATCTGGGTTTGTCTCCCTCGGGTTCC  
GTGAATTTGCTAGAGCAGCTCACAGAACTCAGGAAAACTTAAGTTTAC  
CAGTTTATTCTAAAAGATATTACAAAGGATACAGATGAACACCAGATGAA  
GAGATGCGCAGAGCAAAGCATGTGAGAAGGGGTGTGGAGCTTCATGCCC  
CTCTGGGGCACCACCCTCCAGGAACCTTCATGTGTCCAGCTATCTGGGAG  
CCCTTCCAAACCTGTCTTTTTTGGGTTTTTAAGAGTGGCTTTATTACAT  
ACACATGATTGACCGAACCATTTGGCCATTGGTGACTGACACAACCTTCAG  
CCCCTCCACTCCCTCCAGTGGTTGGGGAGTGGGGCTAACAGTCTCAAGTC  
TCCAATCCTGCCTTGGTCTTTTCTGTGACAAACCCATCATGAAGCTACT  
GCATTGGGGCTGCCAGCCAGCAGTCATCTATTAGCATGCAAAAGACACTC  
TTATTATTCCAGAGATTCCAAGGGTTTTTAAAGCTGTATGTGAGGAAAC  
AGGAGATGAAGAACAAATATATATTTTCAACATCACACTCGTTGGGGGA  
ATTGACAGGATAGCAAACTGATTAAAGGAGGATAGGAGAGACTGAGATA  
TATATTTCCATATATATATATAGAGAGAGAGAGATATTTCCATATATA  
TATATAGATCTAGAGAGAGAGAGATAGAGAGAGAAGAGTCTTTCC

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ACACATTTGGGGGAGCAGTTCGGGAGGTACAGCCCGGACAGGAGATGTGA  
GAAGATCGTGGTTANTGTTCCCTGGTCCAGAACCCTCCAAGTGGGCTT  
AAGTAGGAAGGGTGGTGAGCGGCAGGTAAACACACGTCAAAGGCAGTCTT  
CCTCTCTGAGGGAAAACTTGTATAAGCATTGCAATCAATGGGCCTCTT  
TAATTATGTGCCAGTGGCAAGAGCGGGTGCTGAACCCAGGGGCCTGCCTC  
AATCCGGGGCCTTTGAGGCAGAATAAAGTGGTCTCAGGTTGTTGGCATTT  
CCTTGCCCTTCCACCCGAAGCAGACACAAATCCTCTCTGGAGGCAAGTTC  
CCCAATTCAGCCAGTACAACCTCCACAGACTAAGATCAATCATGTACAAG  
CTCACAGACAAAGGTCAACCAACACACAGAGCAATAAACAAATTCATGAG  
TGACGTGAATGAGAATAAACAGAAACAATAACCACCAGCTGGGATGCTCT  
AAGTCTTCAGCTGTTAGAATTCCTGAATATAGAATAAACTGCCACAATG  
GCAACATGCATCTAGTACTTACTGTGTGCTGGGTTCTAAGAATTTTGCA  
CATTGTGCCAGATACCGACTCAGCTTCACACTCACCCTCCTACTGTGCCC  
TCTTAATTTGCACTAGATTAAAAGGTAGAAAGGAAGAGGCAGCTATTCTG  
TTCTTGGCTGTGCCTCTGGCAGCATGCAAAATGGGCAGTAACAGTGGC

FIG. 4 (39 of 61)

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AGTCACAGGTAAGTAGC TTCTCACAGTGGGAGTTAAAGGCATGGGA  
GAGACGAGCAAGGTTCTTAAAGGGACAGTGGCCAGTAAATGACCAGGGGC  
TACTGGAGTGGCTGCATGGCTCTGTGGAAGCTCAGAGGAGCCTTGGGTCC  
TGCAGGTGCAGTAGCAGCTTTCTGTAGTTCTGATCTCTGGGTCCACAA  
TCTTCCCCGTTTTTGCTCCTCCACTTCTAATTTTGTAACTGACTTCCCTG  
TGTGTACTTCTCTCTGATTGAAATAGCCAGACTGGTTTCTGTTTCCTG  
ATAAGACATTGTCTGGTACGAACACAGTAACTCATTTAATCCGATATCTC  
TATGAAGGAGGTACAATAATTATTCCTATTTTACAGATGAGGAAACACAG  
CAGAAAAATAAAGTCAATTGTCTAAGGTTGCACATTTAGTCAAGGGAAGG  
GTTGATATAACATATAATTATTTAGAAAAACATCTAAGGAAATAAAAGGCA  
TAATTTAAAAATAAAACTAGGCAGGTTTAAAAAAATGAAGTAATCTATAA  
GTAAAAAAGTATAATTGTTGAAATACATATCTTAGTGGATGGGTAAATA  
GCTGAAGAAATGATTAATGAACTGGAAGGTAGTTCTGAGGAAATCAGAAT  
TCAGCATAGATAGAAAAAATGGGAATTTACAAAAGTACACAGGAATTATA  
AAAGAGGTTAAATTATAGGGAGGGTAGAATGAGAATTAACATTGGTCTAA  
CTGGAATTTTGGGAAGAAGAGAATAGAGAGAATGAACAAGGCAATATTTAA  
AGAGGTGGCTGAGAATTTTTTCAAGACCAACACAACTATGACTTTACCAG  
TAGAGAAAAAATGTACACTGAGGAGGATAAATAAATATACTATGAACAA  
ATTGTAATAATAACTCAACAAAGACAAAGAGAAGATCTTAAAAATCAGC  
AAAAAAGAAAGTCAGACTTAGAAAAGAAATGACAATGGCAGACTACTCAA  
CAACAACAATGGAACCAAATTCAGTGAAACAGTATTTTCAAAATGCATA  
TTAATCTATCTTTGAAGAATAAGGTTGAAAAGGTTGAAAATTGCTGCCT  
TATACAAAATATCAACATTAACAAAAAGTAATGAAGGTAATATAAAATG  
TTTTCAATAAACAACAACTGAGAGAGTTTACCACCAACAGCATTCTTA  
AATGGACTTTTAAATGCAGTTTTTAGGAAGAAGGAAAAAATTCCTAAGG  
AAGGTCTGAGATGCAAAAAGGAATTATGAACAAAGAAATTTGTTAAAATTA  
TAGGTGAATTAATAAACTGCCTGCATAAATGATAATAATGACAATGATG  
CTATTAATAATAGAGTTGATAAGGATAAAGAAAAGGACAGAATTAATAAC  
TAGAAAAACAAGCATGCTGGAAGGATTCAGGAATTACTTGAAGGTTAAAG  
TTCTAGGGTCTTCTATCCTTCTAGAGGGGAGTCAATATATTAATTTTG  
ACCGTCACTTACACAGTGAAAACTTTAAGGATAACCTAAAAAAATAGA  
AATAGAGAGTATAACTTCTGAAACAGTCAAGGGAATAATGGAATAAGA  
AAACTGACCAAAAAACATCTCAGTCAATCAAAAAAAAAAAAAAAAAAGAAA  
GAAAAGGTTCCGAAGGAGAAAAATCAAAGCATAGAAAAAGCGGGACAAATA  
GAAGTGGAAAAAGAAAAAGGTAGAAGAAACAGGTCCAGAAATATCACTGAT  
GCCTAAATCACCATTAAAAGATGAAAACAAATGAACAACATCAAAAAAT  
TCTAGTGAAGTGTAGTAGTGCTGATCAGAATAGGCTCTAAGATAAGATGCA  
TTATTGTGAGTCAACTTGTGATGATGAAAGGTTAATTCACCAGAAAGAC  
ACAAATTATAAATTGTAATCAAATAGTTTTATTTTACTTTATTTAT  
TTATTTTTTTTGGAGACAGGATCTTGTCTGTTGCTCAGGCTGGAGTGCAG  
TGGCTTGATCTCAGCTCACTGCAGCCTCCACCTCTTGAGGCTCAAGCTTT  
CTTCTGCCTTAGCCTCATGAGTAGCTGGGTCCACAGGCACACACCACCA  
AGCCCTGCTAATTTTTGTATTTTTTGTAGAGATGGGGTTTCACCATGTTA  
CCAGGCTGGTCTCAAACCTCCTGGGCTCAAGCGATCTGCCCCCTCGGCTT  
CCCAAAGTGTGGGATTATAGGCGTGAGCCACGGTGCCTGGCCTCAAATA  
ACTATTTAAGTGAAAACAAACTAGTATGGCACTAATGAAAAATGTATAAA  
TCCATAATCGCAGAGGGATTTCAACTTACTTCTTTGATTATGTAAAGGT  
CAACACAGACAAAAGACAATGACAAAACCTAATGCAATGAACACTTTTGAT  
TTTTTTGAGTTTATGCAGAACATTTACAAAAATTTAGTGAAGCCTAAAT  
ATAAAAAAGTTGCTGTACGTAGAATAACACACAAACCCCTGAGTCCGGAA  
TTCAAAGCCCTCCACACTCTCCTCTACCTTTGCATCTTTATCCTCCACCA  
CACTGCAGTGCATACTCTGGGCTACTACTCACTGTTCTTGATTCAAATTC  
CATGTTCTGTGAGCTCAAATCATTCTCTCTGCCTGGAATAACTACTTCAT  
ACATATTCTGCTATTGAATTCCTGTCTTAGCACCCCATCTACTCCAAGAC  
GATGTCCAGTTGGGGTTACTCCCTGTCCCATTCTTTGATTACACTTTT  
TTTTTCTACTTCCATTATATTATTTGATCAGATCTGTGCCACAGTTTTTGA  
CTTTGTGTCTGTTTTACTCTTTTCTAGACCCTGAGAGCTCCTGAAGGGT  
TGGGTCAATTCCTTTTTTATTTGCTCATTCTCATGGCACAGTGAGTGCTT  
ATAAATGGCTATTGACTGAAATTAACCTGTATCTAAATGGACATATTC

FIG. 4 (40 of 61)

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ACTTCTGGGCCATTTCATCTTTCTTTCTATTGGAACCAGGAGATGGGGAA  
CCATAACAAAGGTAAGGTTGTGCCATGTGAAAGAACATGGAACCTTCCCC  
TGAGGGCCAAAAAGAGCAGGGAAAGGTGCAAAGACAAAATCTTCCATTT  
TTAAACAAATGTAAGAATGTGGTCCACCTCATGCTCAGGTGGGACTTTATC  
ATGACGTTATTTTTGGGGACTTATAGCTGCATCATTTACCCCATATACAT  
TTACCTTTAGTGTAGGGAACCTGAGGACAGGAATTTTGTGTATGCAGACTC  
TTGCTAATGAGGCTAACACTTGGAGAATTTTTATCATGCATTCAAGAAGC  
TTGTTTACATTTCTTCATTAATACTTTAGTTGGTGGTTTAGCTTTAGTT  
GTAGGCTTATCAGATATTTGGAGATATCTTCATAAACGATGGCTTTGGTT  
TTAGAAGAGTTATTCTGAAGCTACTATTTCTGGCAATAATCAAACAGCAT  
GGCCATTTGTTTTGTAAGGCCCTTTCCTAAATATGACGGTAAATCTACG  
TGTGGAAAAATGCTTATTCTTCTGTCCTCTATAAATGTGAATCTAGTTTG  
TCTTCAAAATGAAATCAAGTGATTAAAAATGTAGTTTTCTAAGAAGATAAA  
TGGAGCAAAGCACTCTGTGTTTCAAGTGTGGAAATCACTCATCCCTCA  
TAAAACTGTCCCACTGATCCTGACTCACATGAATGAATAAAAATAAGAG  
TTAATAACATCAATTTACATTTTTTAAAGACACTTTCCCATGTTTTAGACT  
ATTGGTTGGAAAAGCTGGTAGGTGTACAATTTGTGGAGAGTTGGCTGTTT  
TTGTCTGTCGTTGTTTGACGTATTTCAAAGCCATATCTAATTTTGTGCA  
GAATGGTCTGAATTTCTACAAAAATGTTGAGTTGTGTAGTGTGGAGAAGTA  
CGGAGCCATTTACTGAAAGGCTGGGGGGAAATGACGAGACCCTGAGATAA  
GGCAGTAGTGGTGCGAACAGAGTGGAAGGGAGGTAGTTGAGATATGTTCA  
GAGTAGAATCAGAATGGACATAGTGAACAACCTGGATGCAGGTGGGGGCTG  
AGGAAGCAAAGTTGAGGATAATTCTGAGACTTCTAGGTTGATCCACTGAA  
GTTACATTATTCAACACCACAAGGAACTAGGGGAATGAGAAGGCATACT  
GGTTTGCTTTGGAGTGGAAGGGCAGTGATGTAAGAGGAGTTAATGAGTTA  
AAGTTTGGATATGCCTGAACTTCAATTTGATATGTGCATCTGATATACCC  
TTGGGGTGACCCCTCCAGGCAATGGTTGAACATGTGTATTTCTTAGTAACT  
GATAGGCATCACAGACTCACATCAGTAAGGAAGCAACAGCAAACCTTGATT  
GGACGATATACCTGGAACCTCAGTACCCTATGACTGGAGCAAGTCTCTGTC  
AGTGAAATGAGGATAAGAGAATCTTGACCTTGTGGAATATGTTGTTAGG  
AATATATGTGATGAACAACATAGGATACTTCTACAGGGCTCCACATGTA  
GTAAGGGCTTTATAAATGCTTGATAAATATTATTGTTGTAATTTATTTCC  
AAAGTAAGATGCCACTGGAGGAATCTTTGGAACCCAAATTAATAACAAAT  
AGGACTGGATGCAATGGCTCACACCTGTAATCCAGCACTTTGGAAGGCC  
AAGGCAGGAGGATCTCTTGAGCCCAGAAATTCAAGACCAGCCTGGGTGAC  
ACAGGGAGACCTTGATCTATGAAGAATTAATAAATTAACCAGATGTG  
GTGGTGCACGCCATAGTCCCTGCTGCTTGAGAGGCTGAGGTGGGAGGAT  
TGCTTGAGCCCATGAGGTTGAGGCTGCAGTGAGCCATAATTGTGCCACCA  
CACTCCAGACTGGGTGACAGAGTGAGACCCTATCTCAAATAAATAAATAA  
ATAAATAAATAAATAAGTACAAACCAGCAAACACTAATCCTTTCTAGAGA  
TTATTGAACTCTGGAGGGCAGATCTGAATGGAGCCAGCAGAGGGACCTAT  
GGAGATCAGCCTGGCCCTGGACAGCACCAGGCAATGGGGTTGCTAGAGAG  
GTAATGGGGTTGAACAGGGTTTAAGCCATGAGGTCTCAAGAATCCGTGAA  
GACTCAGACTAATTTTTTTTTTTTTTTCATGAGGATTAGGTGTTCTTAGGA  
ATTTCAATGAGAGCAGGGTTAATGAAGGAATGCAGGGTAGGAGAGCTGAG  
GGAAGGCATCTGAGAGAGCCTGGCTTATGAATGGCTGCGTCAGTATGGCT  
CACCTGCTTTCTTGTATCTACTTAGCAGATGATCCACCCAGGCCTCC  
AGGGCCAAGGTCAATTTCCACATAGTCATGGGCCCTTGAGGGCCTGGAGCA  
GTGTAAGGAAGACAGAGTCTTAAGAAATTGCATTAACAGTCATGGTGCTT  
GGCAAGTGTGTCATCCTATGCCAAGCCTGATCTGAAGGGGTGCATGCTC  
ATAGGTAGCTGCTGCCAAGATTACAGCAGCTTCTTCAATCCCAGATCCA  
TGCTCTCCTATATTCAATTTTCCAGGGGTTCTGTCTTTCGACAGTGATG  
AGATGCAGAAATGACTTATTGAGTTATTCTCCTGATAGTTGCCAACTTTTC  
CAAATGACAAATGGGGCATGGAGCTTGAGAGTGGAATGAGGCCCTAGGGA  
TAGCGTGCTTAGGAAAACACTCCAGCCTGATGTAATTTGGGGGTACAA  
TGGCATTTTCATCATCAAGACTGATGTAAAGGGTGACTAGCAGTGAGTTG  
GGGGTGACTCGCACTGGGGCTAGGTTTCTGATTCTGCCTAATCCAGACAG  
AGCAGAAGCACTAGTGGGCTGGTAGAGGGCCTCCAGGGCCTCACTTAATG  
TCCTGGAAAAACAGCTCCAGATTGTTGGTTTACGTTCTGAGGACAAGCTT  
GGGTACTACAGGATAGAGAGAGTGGTGGGAGATGCCGTGGCCTGCCCTGC

FIG. 4 (41 of 61)

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TGATGCCTGCCCTGCCATTCTCGGTGTGATGTCTCTGGGGCATCTTGCC  
TCCCTGCCCAGACCTGTAGTTCAGCTGAGGGCATGTGGAGGCCAAATGG  
CTTCTTAGAGTGTTACTTTCTTGAACAGCTCTGCTGGGAGAACTGGAGG  
AGCTAGCTAGTCACGGTAACCTGCAGCAGTCAAAGGATCGTCCCGGTGGAG  
GTGGGGTGGAAAGGTAGAGAAAGAGAACATATAGCGTTTCTTGGAGAT  
GTGTGGGCATGTATAGAGGAAATACCCAATTCCTGAGCCTTGAGCCCTC  
CAGGAAACCTTGGAAATATTAGGTAGTTCATCCCAAGGAAGTCTAAGAAT  
TCTGGTCTCACCCATCTCCTTTAATTCCACAAATGATCCTACATGATATT  
AAGGAACACGGGCCAGTAACCTCCAAGCAATGGATGTGGTGGTGAAGTT  
TGACCTCATGATGGAGCGGAGGTGGTTTTGAAACCTAAGAATTTAATTTA  
TTGTTTCAAACCTGTTCTCCACTCAGCGTTATTAAAGCATACATAATTGAC  
ACATAAAATTTGTATATGTCTACGGTGTACAATGTGATGTTTCGATCTAT  
GTATACATTGTGAAATGATTACAACAAGCTAAATAACATACCCATTCTATC  
GTGTTTCAAAGGAATTAAGTCAAGCACAAAAGAGAGGTGCTGTTGAAGA  
GTAGGGCTGCTCTATCTAAGTAGTATGTCTGGGGTGTCTGGATCAGGG  
TCCTTTTGTGCTAGTAATAAACAGCCCTTCTGGGGCTGCTCEACTTTC  
CCACATTTTCTTCTGGAGCCTCCCTAAGAATTAGGACATGGCCACTTCT  
CTGCATAGGCTTCTACTTCAACAAGGACAGGGCTTGTGCTGCCCCATGC  
CACTTGAGTGTCCCTACAGCACAGAGCTGAGTGCACACTGGCTGAGTGAG  
GAAATCCCCCAGATTAATCTTGGTTCTAAGCATCATGGCTGTATTTACA  
CGTATATGAATTACAAATTACAGCATAGTCGAATAAGGATTTTGTGCTA  
CAACTGGAATCCCAGATTATGCAAATTGGATAGTATAATATTGAAATTC  
TAGGACTTTTTATTAGTTTTAAAAAATTATACAAGCTTAGAGTAAGAAAT  
TAAACAGTGCAAAAGAAATTCAGTGTGAAAAGTAAATGCTCTGTCTCTGC  
TGAGAGACAGATATTGCAGCCCAGATACTACTGGGGTCAATAGTTTCCTT  
TAAGCATGCCATTTGATGGTTTATGGGACTTACAGCTCAAGAAGCTTGA  
CACTAGGGTTGATCTCAGAAAATCATTGTTGCAGGTATTAGATATGACCG  
TCTCATAAAGATACACACACAGACACAGCGATTGGAGATATTCACTGGGG  
CTTATGGGCTGCTTGTCTTTCTGCTCTGTGCCTAAGTTGGGCTCAGAGT  
AGCCTGGCATCGGCTGTGGGGAGAATGCTGGCATGGGGTTAGCAGGAGCC  
CACTTAACATGTCTAAGCCACCTGGAAGAGTCTTCAAGGAGACCAGAC  
TCCAGAGGCCCTAAGGAAGGAAGGACTTTTGCCGTTTTTAGGTATTCTA  
GTCCCAGAGTTTAGGGAGGAATGGTTTGGCTTTGGGTGCTGTGCCCCCTT  
ACCGAGTGGGATGGGATGTGCCCATGAGCTGTTGAGCTGGCTCTTGAGA  
AGACAGCAAAAGCGGGAATAAGAGGTGAGGAAGCTGTGTGGTTGTAGGAA  
ATCCCAGCAGAGGGCCTGGGGGTCAAAGTGGTATGGTAGTGACGGTGG  
AGGCTGAGGTGGTAGAAAATCAGAGGACAAACCCCATGGGCTGCTGGTGA  
TCTGACCCAGCTCCTATGCTCTCTGCTTCTTATTTAGGCTCTGTAGCAGC  
AGATGATTGGCTGGTGTGAGAGCAGTGACCTGCCATATCAGGCAATCCA  
AGACAAGTCCAAGCTACGCTGGGAGGAAACCTGAAGGCAGCAGCAGGTAG  
ACTGGCTGAAGACAGACAGGCAGGCAACTTGTCAATCAGATTTGTGTTTT  
TAAGGACTTTTAACTGGGGAGCCCTCCATGACAGATCAGATGAGAGAGGA  
ATCTGGGTCCGCCATGTGTCAAGCTACCAGAGGGTCCCATCGGTGCTTG  
GATCTTCTTTGAAGCTGGGTCTGAGGTTTGCAGGTAGAGGGTGAGCTGGT  
CAGAGGGACCTATTGCAGAGCTAACCAACACCTTCCAGGAATGCAAGCA  
CAAGCACCCACCGCGGGCAGGCGGGCAGGCACTTCTCCTTTTGCCACCA  
GGACCTCACAGAGGCTGATCTGGCTCTGTGAGGTGGGAAAATGGGTTGTA  
CTTAGTACATAGAGATAAAAGGCTTAGGAGGCCCTCCATCCTGTGACCC  
TGTCCCCAGACCACAGGTGCCGGCAGGTGCTGCTATTTCAAGGCTGGGCC  
TCAGTGCAAGCTTGTGGTTTTCTTGCCACCTGTGATGTCTCCCACTAAT  
GAAGGGGCTCTCCATCCTCTGTCTGCCTCTAGCAAGTGGAGGCTCTGGGC  
CCTGGGCAAGACACAGGGGAAATGCCATCTGTTATCCAAATATATTTCA  
ATGTGACAGGAAAGCTGTCTTTAGAGCACAGC

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GCATGTGCTCTACATTGATCCCAGGAGTTTGAACAACATTGCAAGACTG  
GGCAACAAGCAAGACTCTGTCTCTACAAAAATAAAAAAATTAGTTGGG  
CATGGTGGTACATGCCTGTGGTCCAGCTACTCCTAAGTTGAAGAGGGAG  
AATTGCTTGAGGCCAGGAGTTCAAGGCTGCAGTGAGCTATGATCACACCA  
CTGCACTCTANCTGGGTGACAGAGCAAGACCCTGTCTCTAAAAATAATAA  
TCGTAATACATTTTTTTTAAAGTAAAAACAAAAAAGGTCACTTTCTCA

FIG. 4 (42 of 61)

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TTTTAGGGAGACATGAGACATCAGTGAATATATGTAAGATGTACACTGGT  
TCCCTCCAGAAAGGCAGAACAACTTGAAGCAGGGAGGGAGCTTCCAGGTC  
ACAGGTAGGTGAGAGACAAACAATTGCATTCTTCTGAGTGTCTGATTAGC  
CTTTCCAAAGGAGGCAATCAGATATGCATTTATCAGTGAAGCAGAGGGG  
TGACTTTGAAATAGAATGGGAGGCAGGTTTGCCTAAGCAGTTCCCAGCTT  
GACTTTTCCCTTTAGCTTAGTGATTTGGAGGCCCAAGATTTATTTTCCT  
TCTACATCACTGTGGGCAGCTGACTAGGAAAGCTTTGTAGGACTGGTGGG  
CAGTGTGAGAGCCCACTGGGGGGTGGTGGTCTGTGCCAATGGTAGCAAC  
CACCTGTGAGGCTGAGTAAACTCATTTCCTAACCTCCTCTAGCAGCCCCA  
GTGGAGATACAGATGAAGCAGACTAGCGATACAACCCAGCCTGAAGTTTT  
GTCTGGTGAGTGAATGGAATAAAAAATGGGAAGGGTGCTGAAGAGACCAG  
CAAGAAAATGGTTGAAGAGATGGGGCAGAAATTAAGCTGGATCAAAAA  
GGACGGAAAAGCAGAAAGGGCCGATAGAGAGAGGGGATATCTATGGGTTC  
GCGATTCTGAAAAGGACAAATCACTGGTGCTTTGAGAAGAGAGAGGGTGA  
GAAAGCAGGAAGGCTGGAGGCTGTCTATCCAAGAGGCGGACATCTGTGAAC  
ATGATTCCAAGAGTCACCAGACCATGGGGGTGGCCAAAGGGAGTGCCCTCT  
TCTCACCTCCTACTCTTAATTCCTTGTACTCAAGATAATAAGTTCCCAGA  
AGAGAAGTACCCATATTTAATTCATCTGTGTCTTCTAGCAGTACTAAAA  
ATATTATATGAAAGGTATCAAACTTTGAGAAATGTGTGCTGCTAAATTGT  
TAAGGATGCTGGAAAACCTCAAGACGTCCCTGATCCTGAGCCTGAGTATGA  
GCCTGTGGTGAGCCCAATGCAGGTCTCCATTGAGACAAAGGCCTCAGGGA  
ACGGATGAGACCTAGGGACAGAGATGCATGCTGGAGCAGCATTCCCCATC  
CCTACTGCAGCTCAGGCCAGCTGACTGCTTTATGAGTAAACGTTACCAGG  
GAACACTTTGCAGTCTTAACACACATGCCACCTGTGACCACTGATCCCT  
GTTGGGTGACCACTGACATCAGAGATTCGATGGCAGCAATGAAGACAAGG  
CTATCCTCATTAGGAAGGAAAGGAGGAGGGAGGAGGGCAAACGAAT  
CTTTCCTGCTTGTCAACCACGTCCATCTCTGTTAGGTGATTTCCCATGTG  
TGACTTTGTTTATCTTTATAATAACTCTGAGAGGTAGGTCTTGATGTCCA  
CATTTTGAACATGAGGACATCCAGCCAGGAAGTTGAGTTCTGGGGACATA  
GCTGAGAGGGCAAAGCTACATATAAAACCCCTCTTTGTTTTTTCTGGCTTA  
TCCACTGAGTGCCCCCTGCAATCCACCAGCCCATTGTGTAAGTGCATACT  
ATAGGTAAGTTGGCACAGGAGGAGTGATGTGGGCGATTTGTCAAGCT  
CTCCAGGAACCTACACACTGGTGAGGAGGGCCAGGTATGTTCTTGACCAG  
TCACAATCAAAGCAACCTCCTACTAATCAGGAGGCTTGGTACCTGGGGA  
ATGCTATGTTGAAAGGTTCTTTTCTGGGTTTTAAATGATGGGTCTATTT  
CCTTATTCTTAAGATTGCTTTTTTTCTGGCTAGAACTTAAAGAAATTTT  
CAGTAAATTTCCCTTCCCTGGCACAAAGTGAGCTTGAATGAATTTCCA  
GGTGGCCTTGATACTTTAAATATTGCCTCCTATAAAATCAACCTTTAGA  
AGAAGGAAGTCAAAGAACATGCTAGATTTCAAAAGGTTAATTCCTTGAA  
ATCCAGTTATCTACAGGACAATGTTGTCAAAGAAAAAATTATTTGGCCAG  
GCACGGCGGCTCATGCCATATAATCCCAGCACTTTGGGAGGCTGAGGCAGG  
TGGATCACCTGAGGTGAGGAGTTGAGACCAGCCTGGCCAACATGGTGAA  
ACCCCATCTCTACTAAAAATACAAAAAAATTAGCCAGGTGTGGTGGTGG  
GCACCTGTAATCCCAGCTACACGGGAGGCTGAGGCAGGAGAATCGCTTGA  
ACCCGGGAGGAGGAAGTTGCAGTGAGCCAAGTTCAAGCCACTGCACCCCA  
GCCTGGGCAACAGAGCAAGACTTTGTCTCAAAAAAAAAAAAAATTCAT  
GATATTTTTAAATTCATGGTAAGGAAGATTTCAATCAGAACAGCACAGA  
AGATATAGGAAACACTGCAATGGGACTTTGCGGTGGGGGAGAGAGATTGA  
ACACAACTACATATACAGCACGGGCAAGGACATATTCATAGCCAGGAAGC  
AGAGCAAAGATCAGTGGATGCGAAATTACTAAGAGGAAACATGAAAAATA  
AGGGAGCTTCTGCCTAAACCCACCTAACCGGATCCTTGCTGAAGACAGGA  
CAGGGTGATTGGACACCACTTTGGGGATGGTGGAGGATGGGGAATCCAGT  
GAGATTTCAAGGGTGATCAGATATTGAACATAGAAGGTTCTTGCTAAAAA  
AGGAGTTTCAAGAAAGTGTAACAATGTGCCTGGGAGAAGGTTGAGGAGC  
CTGACTAAAAATTTGGTCAAGCAGAGAATATTTGCCAAGATAATAGCTAAG  
TCTTCTGACAAACAATAGATGCTAAGCCAGCAAGGGTGATGTGCTCAGAG  
AAAGCACTGAGGGCTTATTTCTTTTCCCCCAATCTCCACTCAGTCAAGT  
CTAGTCCCCTTGTCAATGTAGCCATTTGTAAGAATGCAATCAGGCAGGGT  
CCCATCTCCTAGTGACAGGACTGACTGAAGTTCTGCTGAAGAGAGTGGCC  
TGGGGCTGACACCGAGATTTGAGAGTCTGGGTTTCGCCGAGAGCTCAGT

FIG. 4 (44 of 61)

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GTAGTGCCATGCCCTCTCTCCACCTGAACGCCAGTGTGGGCAGGAACAA  
CTGCAGCTAGAAAGTCTGGCACTTACGCTGGGGTCTAAGACCTGCCTGATC  
TGCTAACTAGTCTTGTCCCTTGGCTATAAACTGACGTTGGCACCTGGCCA  
GAAAGATGAGCAAGAGATCTCTGACACACCTTTAAGTCCCTGTGGAGTAG  
GATTATGTTGGGAAGGTCAATTCTCTGACTGAGCAGCAATTTGAGAAGG  
AAGTCCCATGCCGAAGTGAGAGAAGGCAGGGAATCCTGCCTAGTCAGCTA  
GAGCAAAACAGTCTGCAGGACGGGACCCAGGGATGTGATCCTCCCATCCA  
AAGGCACTGAACTAAATGACTAAAATACTTTCCAGGGCTCACGTTCTTTG  
AAGAATGGGGACTAAAATAAGACAGGAGCCAGCAAGTGAGGACTTGGAA  
GGAGATGGCTCATCTGATCAGCCTCCACTCAACAATTTAATCATCCACA  
CTGGCATGGGGACACAATATGAATAAGTTGACAGGGACCTACTCTGATTA  
AGCAGTGGGCTAGTGACAGAGACCTGTCAGTCAAGAGTGGACAGGAGATGA  
TTTCAGACAGTGAGAACAATAAATTAACAGAGTCATGTGCTAAAGGGTGGCT  
GGAATAACAGAGGAGTTTAAGACTCAAGAGGTCTGGCTGGGCGCGGTGGC  
TCATGCCTGTAATCCCAGCACTTTGGGAGGCGGAGGCGGGCGGATCACA  
GGTGAGGAGATCAAGACCATCCTGGCTAACGCAGTGAAACCGEATCTCTA  
CTAAAAATACAAAAATATTAGCCAGGCGTGGTGGCGGGCACCTGTAGTCCC  
AGCTACTCGGGAGGCTGAGGCAAGAGAAATGGCGTGAACCCGGGAGGCAGA  
GCTTGCACTGAGCCAAGATTGCGCCACTGCCCTCCAGCCTGGGCGACAGA  
GCGAGACTCCGTCTCAAAAAAAAAAAAAAGACTTGAGGGAGTTGTTTATT  
TTTGTCTTTCTTTTAAGACAGGGTCTTTGTTGGGCGCGGTAGCTCACGCC  
TGTAAGTCCCAGCACTTTGGAAGGCTGAGGTGGAAAGATCTCTTGAGCCCA  
GGAGTTTGAGGCCACTCTGGGCAACATAGCAAGACACCGTCTCTACAAAA  
AATGTGCAGGTTGAGGCTGCACTGAGCAGAAAAACACCGCTGCACTCTAG  
CCTGGATGACAGAGCGAGACCCCTGTCTCGGAAAAAAAAAGAAAAAGACA  
GGGTCTCGCTGTGTACACAGGCTGGAATGCAATGGTGCAATCATGGTTC  
ACTACAGCCTGGAATCCTGAGCTCAAGCAATTCTCCTACCTTGGCCTAC  
CAAAGTTCTAGGACTACAGGTGTGAGCCACCACAGTGGCCTCAGGAGAG  
ATCTTAATAATAAAGGACAAATTCCTTGATCCCTTAGGGGCAGGATT  
GACACATCCAAGGATCAGGCAGAAAGCCTGTGCGGAGTGGGATGAGCAAA  
GAGAAAGGCTGAGAGTTGTGAAGAGGGAGATGCAGTGCCAGCTAGGACAG  
GCCTTTTTGGGCTATGGGAGGTTTTTCAGAGGAGACCCACCTAACTAAC  
CCATAACATTGCAGTGGGGACCTGTTGAAGTCATGGAATACTACCTGAAA  
GCCAGAGAAATGGGAGGAGCCTTTCTCTGAGGAGGGACTCTAGTCCATA  
GGTATCTTGCCACCAAATACATGGACAGGCCCTGGGGGAAGATGGTGGTA  
GCCCAGCTGGAGGAAAACCATTTGCCACCTGAAGTACCCAGGGTAAGCC  
ACCCAGGCACTGAGGCTGCACACCCATGCATGCACACAGAATCACACT  
CCTTCCTATTATTCCTCAATTCAGGGTCTCAACACCCATTTTTTTGTT  
TTTTGGGGTTTTTTTTTACATGTTTTACATTTTATTATTATTATTGTTGA  
CAGGGTCCCCTCTGTTGCCAGGCTGGAGCAGTGCACTCGTGCAATC  
ATATTAGATTGGTGCAAAAGTAATCACGGTTTTTGTCAATAAAGTTTTG  
CCATTACTTTTTAATGATAAAACCACGATTACTTTTGACGCAACTTAAAA  
GCTCACTGCAGCCTCAAAATTCCTGGTCTCAGGGAATCCTCCTGCCTCAG  
CTTCCTGAATAGCTGGGACTACAGGCACATGCAATCCTACCTGGCTAATT  
TTTTAAAAATTTTTTTGTAAAGATAGAAAGTCATTTGTTGTCCAGGCT  
GGTTTTCAAACCTCTGTCTTTGTGCTCCCTCTGCCCTGTGCAAGACCTTC  
TGGATGCCCATAATGAAGACTTCAGGGAGAGGAAAAAGTAAACATAGGT  
CCCTGATCAAGGGACCAGGGTTTATCGACCACAAACAGCATGCCAGATT  
CCACTGGCAGTCTAGAGGTGCAATTTGCCCAAGTGTGTGTGGAAGGCC  
TCTCCCTAGCAGTTGGTTTATACACCAGCCACAGCACAGCATATTCTCTT  
AAATTGTGAACATTTGCAAAACTCCTTGAGGACAATATCATGTCTTGT  
GTACTTTTGTGTTTTGTTTTCCCTTCCCTATGTACACGCGCGCATGCACT  
CATGCACGCACGCGCGCGCACACACACACACACCCCTCAAACCTGAA  
TGCCTGGTGTGCTGAATGGATGAATGGCTAATGTAAGTCATTCTAAAGC  
TACTTTCTTTGGCATACCATCACCTTTGATTTTCATCTTTCTGGAACCTCT  
ATGTTCCCAGATGAATTTGGAAAGCCCTCAGGAAACATTTCAAATTTGCT  
ATATGGGAGAAATGGGAGGGTCTCTCTAGAAATTTACCTGCCACAGGTAT  
TTCTGGTAAGACACAGCAAAGGTGGCACCACCCATTCCTCGTTACAATGT  
CAATGCCAGTCACCTTCCTGTCCATAAACTTTATTAAAGGTGCAGAAAT  
TCCATGGAAGCAGGTGGACACCATCTGCTTCAGCCAGCCAGGGGAGCA

FIG. 4 (45 of 61)

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AGGTGTCACCTGCTGCCCTTTGTGGCAGGAAGCTGCGCTTCTCTACTCTCCCA  
CTTTGAGGCCCTCTGGGGCTGGCCCTGCTGCCTCCTCAITGACAAGGCTGCT  
TACTGAGCAGTTTATTCTGAGCTGGACATAGTGCTTCTGGTGAGTCTCTA  
CTTCTATTTAAACCCAAAGATATTCTTTCTAAGGAAACGCTTTCTGTGCG  
GGGGAGGTTAGCTCCAGATGGAAGTCACAAGTGATGGCATGGTAGCTCTC  
ATCCGTTTGGGTGGATGATATTACGGAGCACCACCATGAGCCAGTCA  
GAGGTGAACAGTATATGCCAGCCCTGAATCAGGTGCATTGACAGCAAGGG  
AGACAAGCAAAACAAAGCTGAGGTTTGCTGAGGATGTTCAAGACTCACACA  
GCACAGAGGAGCATCCACCACCCAGCTTGGGAAAGGACTTGTATAGAGG  
GGGTGAAGCATGAGCTGAGTCTTTGAAAGACTAGAAATTAGCCAAACTACA  
AGGAGGAGAAGGAGTTTTCAGTCAGGAAGAACAGGTTATGCAAAAGCACA  
GAGACTAGAAAGAATATCACATTCAAGGAAGTCAAATAGACAGGAAAGA  
TTGATGCGTGGGATAGGAGAGGAGGGCAGGGGATTCCAGGTGGGCCCTGC  
TTGCCACACTCAGGAGCTTGAACCTATCCACAAAGGAGGTGTGGAACCA  
TAATGAATGGGTTTTGTGCAAGGGCTTCATGTCAACAGATTGTCTTTTG  
GAGATACTTCTGTGGCTGATATGTGAGGAAGGGATGGAGGAAGTTTCCGT  
GGCAATCAGGAAAACCAATTAGCAGATGATTCAAATGGCCTAGGGGAAAA  
GGGAGGAGGACTTGGACTACCATGTCAGCAGCAGCAAAATGGAGAGAAATAAC  
AGATCCCAGGCACCTCAGGAAGCGCTCAGAATGAGCCCTTCAAAGAAGTTA  
TGGTAGGTGATGGATGGATGGAGTGTGAGTCCTGGGATAGCATTGCCTGG  
GAAAAACTTTCTAGTTGAGACAGGGAAGTGGGCCAGCAGAAATGGAGGG  
CTTCTTCTTTTTGCTTTAAATACTTTTATAATATTTGGAAGTTTGAAAA  
GAGCAGATATATTAGCAAAAAGCCTAAAAGGGATATTTTGAAACTCTG  
CTAGTCTTAACATATAACTTTTTCAGCTTGACACATCATCAATTAACCTTG  
ATAGCGCCTTTCTGAAACTATCATCCCAATAGCAATCCTTGTAATAAACC  
TATTTTGAAAACAGGGCCTTGTAGGATAGCCTCAGAGATGTTTTGTGGTA  
GATTTTTCTAACCTTCTAATGTCAAGGAGTGAAAGGAATCCCGTTAGAAGT  
TGGAAAATTCTGGAATCTCTATTTCATGGTATTAAGTTTTGCCGTACAC  
AAAAGTTTAAACACCTTTACACAATCAGACTTCCTCATTTTACATTGCTCG  
GTAATTAGAGGAAATCAGTCACCCAGAGCCTGGGTCTAGACTTGACAAA  
ATGCACCCAAACAAATCCTGAGTGGCCTTGCTGAGGACTTCTCCAGAGA  
TAGAAAACCTCAGTTCAGCCAAACAGGGGGAAGCAGCTGAAGAAGTGAAA  
TTAACAAAGTCTTGGAAGGAAATGACCAATCATCTTTGATTGTGTAATA  
ACCAGAGAGTTAGAATACAGCTACGACAGACATTTTGGGAGAGAAGCATT  
TATCATAGCTTTTGAAGAGAGAATATTTTTCAGCATCATAAGCACACAATT  
CCAAGACAGATACTTTCAAGGGATTGTTTTGACG

CACCAGGCCCCACCTCCAACATCGGGGATTACAATTTGACATGAGATTTG  
GGCTGGGACACAGAACCACAAACATACCAGAGTGCTTTCTCATTCTTTTCT  
ATAGCTGCCTAGTATTCTATGTCCTTTACTTCATTTAGGCAGTCTCTTGT  
TGATAGACACTTGGGTACTTCCAATTTTCCATTACAAATGATGTGCA  
ATGAATAATTTTGATCATTTCATTTACATGGGTTATGTCCATCTGTG  
GGATAAATCTCCAGGAGTGAAATTGCTGGATCAAAGGGGAAGTGCACCTG  
TGATTTTCATAGTTAGCAAATTTTGTCTATAAGGGTCATATCAATTTAT  
AGTCCACGCGTAATATTTAACAGTGGGGATTTCCTGACAGTTTGACCAA  
CAAGTCTGTGTAAACCTTTTGATTTTGTCAATCTGATGGGAAAATAC  
TAGTATCTCAAAGTGCTTTTAATTTGACTTTCTTATTACAATGTTAAGCA  
TCATTTTACTCTGCCAAGATCAAATAGTATTTTCTTTCTGTGAACAGA  
CTGTTAAGATCCCTTGCTCTTGTCTTGTGGATTGTTCTTTTCTTTTCT  
CAAATGTTTGTAGGCAGTCTTTTACATGTGAAACAAGTTATCTCTTTATC  
TGGGGTGTGAGTTACAACTACTTTTCTCTGGCTTGTCTTGTGCGCTTTGAC  
TTTGCTTCTGGTGATTCCCGCAATCTGAAAGTGACTTTTGCATCATT  
CATTCTTATACCCCATGCTCTTGTTCACGCTGGTCTCTAECTGAGGG  
CTTTTCTTTTCTTTCTTCTATCTGGGAACATTTTGTAGACAGGGTCTCA  
CTCTGTCTACCCAGCTGGAGTGCAATGGTGCGATCACAGCTCACTGCAGT  
CTTGAACCTCTGGGCTCAAGCAATCTCCAGTGTGAGCTTCCCAAGTAGC  
TAGGACTACAGGTGCATGCCAGCATGCTGGCTGATTGTTTATTTATTT  
ATTTATTTTGTAGAGATGGGAGTCTCACTATGTTGCCAGGCTGGTCT  
TGAACCTCTGGGCTCAAGCGATCTTCTGCCCCCTGCCACCCAAAGTGCTG  
GGATTACAGGCGTAAGCCACCATGCCAGCCCCATGTGTGGAAATCTTCTG  
TTTATCCCTTTAGGCTTGATTCTTATGTCTGTTCTCTCCCTCCTTCTGG  
CTACTCCTCTTGTCTTTATCTTACTCTACTTGTCTGTTACCTTGTCTC  
TGCTTATAACTAGCTGCCTCTCTATCTGAGGAGGAGTGTGACTGTTT  
TCATCTCTGTACTCCAGGTCTTAGTACATAGCGCTTGTCTCAACAGATGT  
TTGGTGCATTGATAGATAAATCAATGGTAGCTGTTAATACCAGTCTTGAC  
TCCCTGCAGTGCTTCAGCTGATCCTGTTCCAGATGTGCACTGAATATCTT  
TCTGTTGAACAACAGAAATAAAGGGGATGGGTGAGGAGGATAGTCTTCGG  
TGGCCAAGGATATTTGTAGGTACTTTGCAGCACTCAGCAATGAGGAGTGG  
GCTTTAGTCCCCCAAGAACTCTCACAGCCCTGTTGTCTTTACTGTTTCTC  
TGTCAAATCCAAGACAAGTCAATGATCAGGAAAGACCTTTTTTTTTCTTC  
AGTGAAGTTTATTTTCAAGACATTGAACAGTATGATATTTGCTCATTAT  
AAATATTTCCATTTAAATAATCTGAGCTTATATATTTTCAGTCTTAATTA  
AAGGACTTGATTTAAAGAGAGCACACCAGTCCAAATTGAATTGATTCCAT  
AGCTATTAATAAAGTAGGCTCTTTTACAGACACTGCTACTTCTTGGCCCCCT  
TTGAATAAATTAGACCAATGAATAAAACAAACAAATAAATAAATAA  
ATAGGGAAGCGGTTGCTCATCAGAATGTGGGAGCGAATGACAGAGGGTTT  
CTTAGAACCAATGTGGCCGTGTTTCTGTGAGGCGGCTTTAAGTGAGT  
AGGAGAGGTGAGAGAGGCTGGCTCAACAAAAGGGCTGGGGATTGGCCCT  
GAAAGGAGAGAGCTGACTGTCTGGCTGATGGACAGGAGATCCTCTTAGC  
ACTACCCTAAGGCAGGCTGTTGGGCATTGGTGTAGACAACAGGAAAGTCC  
AGGCTATAGCCGTACTCAAAAACCTTTCTGTTCCCTTTCTGCCAGCCCTA  
GGGATTGAGTCCACATTCAGCACAGGACTCTCTGGGTACAGCTCTCTTTA  
GGAAGACACAAATTGCATGGTGAAGTCAGTTATATCTTGCCGCTTTTG  
TCCCTCCAGGAAGACGGGCATGTTTTCTGCTTGAGAGGTGCTGATGTAC  
CAGTTGGGGAAGTGGGCAGACTCAAATTCAGCTTGTATTGATTCTAT  
CTTGTTGAAGACAAATCGCTTTTCCATCTTCTTCTTGGGTAATTTTGG  
GATCTACACTCTGCAGCGAAAGAGAAAGAATTTTGTGGGGCAAGGG  
ACAAAAATGCTATGGGAAAGATGTTCTTTGGGTGGCCAGAAAGGAACT  
GACGAGCAGGTACATGATCAGGAGCCCACTCCTGAGTTGTAAGTGGGC  
CCCCAATTTCTGTGTGATTATTAAGAGAGCCCTTCTTCTTTCTAAAC  
TTAGTGCCAAATGCTGAGGAGCATAATGTAGGTGAGAATTTTTTTTTTT  
GGGGGGGTGAAATTAAGCTAGAGCTTCTTGAAGTACCTAGTTTCCAGGG  
GCTTTTATTTGATTTTCTTATGGTCTAGAATGACATCAACTGGAA  
ATGAAGCTTTTGTGAGAAAGCTGGAGGTGATAGTGGTGGTGAATTTGGG  
AGTGGAGTGGACGTGATAATGGGACCTTTAAGTCATCTATTTCCCAAGG  
TGTCTATCAAATGAGAGCAGCCCTAACAATATATAATCTGTTGGGGTTGT  
AACTATGGTAGGACATAATAACATCGGCAAAATGATTTAATTTCTGCAG

FIG. 4 (47 of 61)

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CAGGATTGAAGGTTGCAAGCAGTTAAAAAATTATGTTAAATTTATTACAT  
TAATGCAAAATTGTCAAATAGACCTGTTCCAGCTTTTCTAGGGATGGG  
GGCGGGGAGAAGGTGGTTGTCTGGGAATAAGTGGTAGCAGGAGGCTGAGA  
AGGGCTTCATTCCATAGCATTCACTTACCTCCAGCTGTAGAGTGGGCTTA  
TCATCTTTCAACACGCAGGACAGGTACAGATTCTTTCTTGGAGGCCAA  
GGCCACAGGTATTTGTCTTACTTTCTTCTCCTTGTACAAAGGACATGG  
AGAACACCACTGAAGAAAGAGGGGGTCTTGTGGTTAGGGACACAGCAGT  
GCAGGGTCACCCCAACCCCTAGGCCCATGAGTAGGATACATGTAATTTG  
GTAGCCTCTGTGGGAACCCACAGTGAGGTTCTTGGCCTAAGACACAGGA  
TAACTTGACTTCTCACAGACAATAGCAGGGTCATTTGTGATTAGGGT  
TTCCCTCAAAGGCCTGAGGGTTTCTCAGAGCCTCATAGCAGTAGGAACG  
GAGAATGAAAGAGGGTCTACATTTTAAATGCTGAAGGAAGGAAGGAAGGA  
AGCCATTGTGTCACTGGCTGGCAATGTGCCATCCACAGGAGCGGAACAA  
CTTGATCAATGTGGAAGGAAGGAAGAGGTGAGGCTGTACTTCTGCCAG  
AAATCAGGCACCAGAACTGTTTTCAGGAACAGAGAGTAGCCCATGGGAAGA  
AACTGGGAGAGGAGAGGCTGAGCTGGGAAAGTGGCTCCAAAGAGAGACAC  
TCATTTTGATCTTCTCAGTCACAGCAGTGTCAATTGGAAGGCCCTGGGA  
TCACTCTTACTACCCGATTCCAAAGAAACAGGATTTTCTTGGCCTGGCTG  
AGAGCAAATAGCTTCCCCCTTGAGTGAGGCTGTCTTCAAAGTCAGCAGC  
CTTAGTTGCCACACTCCTGTGCAGAGGCTTGGCTACTGTGGCAGATG  
CCAGGCAGATCACCACAGCTAATGATGGGTTCAACGCACTTGAAACTTT  
GCCCCCTACAGCGGAGAGATATAAGTTCTGTGGCGGTAAAATTTCCC  
TACAAGGAACCACTGGCATTTGGGTGGGACGGATGTTGGGGCAAGGGGG  
AAGACTGGGAGGGGGATGGACACATTATCGCTCCAGCACTCTTGTTC  
GCCTCAACAACAGGAAGAGAGAACCACAGGCAGTTAGGCCATGTCCATC  
AAATGACCCCATATTGTGGAAGAAATTGACATTGCACTATGCCAAGAGAC  
TTGGGTGGACATGGTCTGGGAGTGCTTGAGCCGTCTAATTTCTCAGGGT  
CACACTCCTGTTAACAAATGCACTGGCCAGTGCAATCAAATGTGCCATTT  
CTAGGACCAAAGTTTGTATATTCTTTTAAATATTTTTTTCACTTGTGT  
TGATCATTTGCCCTTAAATTAACCTTTCTACTTTGTTTAAACATGGAGAAT  
TAGCAAGCTGCCAGGAAGCCAGGCAGGGAACAGGATGTTTCCATTTAC  
CTTGTGTCTCCATATCCTGTCCCTGGAGGTGGAGAGCTTTCAGTTCATAT  
GGACCAGACATCACCAAGCTTTTTTGCTGTGAGTCCCGGAGCGTGCACT  
CAGTGATCGTACAGGTGCATCGTGACATAAGCCTCGTTATCCCATGTGT  
CGAAGAAGATAGGTTCTGAAATGTGGAGCATGTTGTTTAGGTATAAAA  
TCAGAAGGGCAGGCCTCGTGAGGCAAGGTGGCAAAATTTGATTTCTTGGA  
GGACACCTGAGCATATACGGTCAAAGTCTGATGACAACACCAGTAGGGAT  
GAAGCTGGAGTGGGGTGGCTAAGAACACTGGACCTGACACTATTAGACA  
TGGGTTCCAGCTTCAGGTCTATTACTGCTCACTGTGGCCGAGCAACAGAG  
CTACTTAGGTAAATGGTGATGGTCATAACACTAGCCACAGGGAGGTTA  
CGAACCTCTGGTGACAATGTAAGTGAAGGCCCTGAGAAAGAGTGAGGG  
AGTTGCAAAATGTCAGTAGCCATCAAGATCTTCTTAAAGATAGTTTCCAC  
TAAAGAGATGATTGCTTTGGTTTCCAGCCTTCTTTGTTTTGTCTCCCGC  
TGGGCCTTCTACCTTTAAAGGGCTTTGGCTCTGGGGGAATTGAGTTGGCT  
TTGGCTAACTACCTTCTTCAAAGATGAAGGGAAGAGGTGCTCAGGTCA  
TTCTCCTGGAAGGTCTGTGGGCAGGGAACCAGCATCTTCTCAGCTTGTC  
CATGGCCACAACAACCTGACGCGGCTGCCTGAAGCCCTTGCTGTAGTGGT  
GGTCCGAGATTCTGAGCTGGATGCCGCCATCCAGAGGGCAGAGGTCCAGG  
TCCTGGAAGGAGCACTGCGGAGAGAGCGAGGGAGGAGCCTGGTGAGGTG  
GTCCTGCCAGGAACCATGCTTTGACATCAGAGAGTAGAAAGCTCAGAGAG  
GAGGAAAGGGCTTGAAAGAATCCCGAGCTTCTAAAGATCATCCCTCTCTG  
GGCCAGGCGTGGTGGCTCATGCCTGTAATCCAGCACTTTGGGAAGCCGA  
GGTGGATGAATCATTTAGGTGAGGACTTCAAAACCAGCCTGGCCAACATG  
GCGAAACCCCTTCTACTATAAAATACAAAATTAGCTGGGTGTGGTGGG  
GTGCACCTGTAATCCTAGCTATTCAGGAGACTGAGGAAGGAGAATCGCTT  
GAACTCAGGAGGTGGAGGATGCACTAAGCCAAGATTGTACCACTGCACTC  
CAGCCTGGGCAACAGAGTGAGACTCTGTCTATAAAACAAAACAAAACAA  
AACAAAACAAAATAAAATAAAATAAAAGATTATCCCTCTCTGAA  
GCTCAAGGAGGTTAAGGGTGTACTCAAGGGCACACAGCAGGTTAGAGGCA

FIG. 4 (48 of 61)

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GACTCAAGACTAGAATGAGGGCTTTCTGACACCTTACAGGCTATTCTTTT  
AGAATAAATCCCATTTCTACTTTGTTTATCTTTTGTACATGCCCCACC  
TACACCATACATGTATACCTTCTCTATATCTTTTGTATCCCTAATGCTG  
TCACACTATGATTTGCTTTTTCATGCAGATGACCATAACATTTTCCATT  
ACCTATGCTCACTCAGCAAGTATTCAATTTTCTACACTGTTCTTTTTT  
TCCTTTTTTATAACACTGTCTCATAGGCATTCTGCAAATCCTGTGAGAGT  
ACTTTTTGTGAAATGTTACCCTTTCTCTTATTTCAGAGAAGCTCCGTAT  
TAAGGCTTCACTGAGGTTGCCTTAAGGCATGATAATGGTTCAAAGGCTTG  
AAAGACAGTTAAAGAGACCTGTAAGTGCACAAAAGAAAGTTGAGCAGGAG  
AGAATTTCTTGCCTGGAGCAGAGCCAAGCTACTGGAAGAGGCAATGGGGG  
CAAAGGCCAGGCAGACAAGCCAATGGGCTCCTCCACAGCTGCAGCCAAC  
AAGTTATGCCAGTCTTAAACCTTCTAAAGAAATATGTTTTAAACAAGATT  
GAGGACTGGATTATGAGGCTAGGGGAGGCTATCACAACCTGGAATAAAAT  
AAAGCCAGAGAAAAGTGGCTGCCTTCCAACCTGCACAACCTGACCTAGCTA  
GGCTGATGGCTGGGCCACCTAGGAAGGCTACTGAGCATCATATAAAACAG  
AAGGGACAGCAGGAATATAACATGGCTCTTTGTAAGGATGAGTCTGAAAA  
ATGACCATTTGCTGCCCAAATGCCCTTAGCTACAACCTGAAAATATTTTCA  
AACTGGAGGTTGCAGGATGCTGGAATCTCAGAGATCATCCAGCTCAGCCC  
TTTATTTTTAGATGAGGTCCAAAGCGGGTAAATGACTTGTCAAGGTCA  
AACAGCAAGTGAATGGTTTTCTTTCAAGTCTCAATTCATCTTTTTGTTTA  
TATCATCTATGCTTGTGTTTATAAGCTTCAACCCAGGTAGCAAAAACT  
ATTCTACTCAAAGGGGTAGACATATGTTAGTTCTCAAGATCATCTCTTG  
GTTTCAGAGTTTAACTCAAGTGATTGGCATAGGCTGAATCCATCTCTTAA  
AAGGATAATCAAATTTATGTTGAAGACTTGGTTGTCTTCTACTATGAAA  
TGGGAAACATTATCACTACTCCTCCCTGTCAACCAAGTGTGGCCACC  
ACCACCAACGTTAGTGAGTGACTGTGGTGATGATGACCAAGTGGCCAG  
GTCAGCAAGTGGTGCAGCCTGTGTCTCACTGGAAGAGGTTAAAGTCTTTC  
TAAAACAAAATACCATGGCATCAAAGTGGCCCAAGTCCCTTCTTTGAG  
CTTTCCTGTGTTAGAGCCCTTCTTGGGTTGGGAGTTAAACCCATAGTC  
TTACCTTCATCTGTTTAGGGCCATCAGCTTCAAAGAACAGTCATCTCTCA  
TTGCCACTGTAATAAAAAACAGGGACATGTCTCAATTATGTCTTCTAAACA  
GGTTTATTTTTCTTCCCTGTGTACAAGACTTGACTGTTTATAAGAACT  
GCAAAACAGCCTGCCTCTCAAAGCTGCCTGAAACACCTGGCAAGTTTACA  
GTGATATGCCGAGAACAGTCCAGAAGGCAGATTCTAGGCCTGGCAGGTGG  
GCACCCCTGGGTGCTCCCTGTGATCTTGAGGCCTAACCTTAGCCACAGC  
AGAGTCAGCTAAATCTGAGCTCTCCCTCTCCCTCCAAGCCACACTTTC  
AAAGGGATTCTTGTATTGTGGCTTGAATCTTTTCTCCCCATTTGCCT  
CTGCAGGAAGCCCTTGCAACAACACATCTGGATAGCCTCCAGGTCCAAG  
CTTGGAGGGACTTGTAAATGGGAAAGTAGTCTTAAATCAGATTTACTTGG  
CACCCTGTTTGCCACTGAAAGAGGCAATTTAGGGGAAAAATCTGGTCTCC  
AAGCACAGATAACACTCTACTCTTGAAGAGGAGACCTGCTCATGTTACT  
GGTCTCAGCGTCTCCACTGACCTGTAATAAGCCATCATTTCACTGGCGAG  
CTCAGGTACTTCTGCCATGGCTGCTTCAGACACCTGTGTAAGGAGAGAA  
AATGAGTGACTTCCCATGACGGCTACGTTTATGTGTGATTTCTCTCAGC  
ATCCAGTGATGGCAGTCATGCAAGAAATGATCTCTGAGTAAATGAATG  
AATGTGTGAAAGAGAAGTCTTTGGGTCTAGAGAAAAGCATTTGCTAAAC  
CAAACCCCACTAGCAATGTATTGGCTAGGAGAGCTGGAGCAGAGGCTTT  
GACACTAACCTTTAGGGTGTGAGCTGTAGATAAGCAGTATCCATTCCCA  
GAATATTTCCCGAGTCATAAGCATTATATTACCTGGCATTTTTCAAA  
AAGCTGAGAGAGGGAGGCAGAGAGGGAAGGAGAGGAGAGACAGAGAAAG  
AAAGAGAGAGAGAGAGAGAAATATGCATACACACAAAGAGGCAGAGAGACA  
GAGAGACTCCTTAGCACCTAGTTGTAAGGAAGATTAAAGTCATACTTGA  
GCAATGAAGATTGGCTGAAGAGAATCCAGAGCAGCCTGTTGTGCTTGT  
GCCTCGAAGAGGTTTGGTATCTGCCAGTTTCTCCCTCGCTGTTTTATAG  
CTTTCAAAGCAGAAGTAGGAGGCTGAGAAATTTCTCTGTTGAATACCTG  
ATTTCACAATCAAGTTAAAGGAAAGGGGAAAGAGTATTGGTGGAAGCTT  
CTTAGGGGAGGGGACTAATAAACTGAGATAATTCTCTGGTTTATGGAAGG  
GCAAGGAGTAGCAAACTATGACACATTTGCAATGTATCACCATGCAAA  
TATGCAATGTTTTCTGACAATCGTTGTGCAGTTGATGTCCACATTAATA  
TACTGGATTTTCCACGTTAGAAGAATGTTTAAATTTAGTATATGTGGGA

FIG. 4 (49 of 61)

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CAAAGTGGGAAGACACACAGATTTATACAAGCACATACTTTTCTTCATTCA  
CTTCTTTTGTACTTAAGTTTAGGAATCTTCCCACTTACAGATGGATAAATG  
GGTACAATGAAGGGCCAATAGCCCTCCCTGTCTGTATTGAGGGTGTGGGT  
CTCTACCTTGGGTGCTGTTCTCTGCCTCGGGAGCTCTCTGTCAAATTGCAG  
GAGCCTCTGAGGAGAAAATTGACCTTTCTTGGCTGGGGCAGAGAACATAC  
GGTATGCAGGGTTCAGGCTCCTGACGGAGTTGGGGCAACCCTGGAGATAA  
GCTCACACAACCCTGCAAGACCAGGTGCTGTTACCCTAGCCAATCTCATG  
GATGAACCAGATCAATGCCAGATGAGCTCTGCCTAAAAATGATTTTTTGGT  
GAACTCTGAAAAGTGGAATATTGTTTCTGTAAGAATATCCATCTGAGACT  
CTATCTCTTGGTAATACCAAGAGTTATCAGTTTCTCTTTAACCGAGACAC  
CAGCAAAGTGCCTGCTCCAGGGTACTGCCCAGGGGAGCCCTCCATTTGTA  
GAATGAATGAGAGTCCAGGTTATGAACAGTGCCTGGAGTGTAGGAACACC  
CTCCTTTGCCTCTTTGACAGGTCTGCATCATAACACTTTTTTTTTTTTTT  
TGAGACAGAGTCTCACTCTGTGCGCCAGGCTGGAGTGCAGTGGCACGATC  
TCGGCCCCCTGCAAGTTCGCGCTCCCGGGTTCACACCATTCTCCTGCCTC  
AGCCTCCCCAGCAGCTGGGACTACAGGCACCTGCCGCCACGGCCGGCTAA  
TTTTTTGTATTTTAGTAGAGACAGGGTTTACCATTGTTAGCCAGGATGG  
TCTCGATCTCCTGACCTTGTGATCTGCCCGCTCGGCCTCCAAAGTGTT  
GGGATTACAGGCGTGAGCCACCGTGTCCAGCCTGTAAACACTTCTTATAGC  
ACTGAGTTGAAACCTTGCTCCTCCTGGTTCCTCCAGGAACTGAAATCTT  
TTTGAGCCAAGTCTAGCACAGTGCCTGGCATGTACATTCAAGTGGTAGAG  
TTTGCTGCTTGAATGGGTGAATGGGAATTTGACAGCATTTTTATTCAAAT  
TAGTATGTGCCAGGTATCGTGCTCGCTCTGCATTATCCAAGGGAGTGAGC  
CTCTGTGCAAGTATTTGAGACACGAGGAAATAGGTTCTACTGTGGGAAA  
AAGAGCATTTTCATGGACTTGCTCTCCAAGCAGCCTTCTGATTTTTAATTT  
GGCTCCCAGTATCTTGATATCAGGAGTCACTCACAAGAACTCCATCTTTA  
GTAAGTTATATTTTCCACAGGAAATCTAAAAGCTGTTCAACATGTTAGTT  
TCCTGTGAATTTGATAAGCCATAATCCATTCCTAACACTGAGCCCTCCTG  
AAATTTGGTGTCTGGTCTGCGATAGCTAAAAGCCCTGTCTGGGTGGCC  
TAGGGGACTCCTCTGTTTTGCCTCCACAGGATCCACTTTGCAAATTAACC  
ACTGGTTCTCCGTTGTAGGAACTGCCACCTTCTCAGAGCCTGTCTTTC  
TTCCTTCTTCTCCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTT  
TCTTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTT  
TCTTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTT  
TTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTT  
TTTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTT  
TTTGTCTCTCCTCCTTCTCTCTCTCTTCTTCTTCTCTCTCTCTCTCTCTCT  
CCTAGACAGGATCTACCTTTATCCCCAGGCTGGAGTGCAGTGGTACAAT  
CATGCATTCAATGCATGATCACAGCAGCCTCAAACCCTTCTCAGAGTCT  
TTATGCGGCAACCAGCAGGGTCTGGAGGGTTGGTGGCTCTGTGAACCTCTC  
CTGACAGAACACAGAGATGTCTTTGGTCTGTTGATGTGATTACAAGCTGA  
ACGAAGGAGGATCAAAGCCAGTGACAGGAAGGGAGATATGCAAGGGACCC  
GAGCATCAGCTCTGAGTTAGTCCATTCTGCTTCTGGGACTTGGGATACAG  
GTCAGAAACCTTGAGCTTCTACTTCTCCATCTTCCAATTGTAGCATCCAG  
GACCTCAGAATCTGCCAGCTAAGAGGAGCCCTAATGATTGTCTGGTGGGA  
TATGGTGGGACCACAGAGATGAAGACATGAATAGCTATTTGAATGTGAAC  
AGCAGACGAAGAAATCAAGGCTAGGAGGGTGAAGTGAAGTCAATCAATAG  
CACAGTGTGGTTGAAGCAGCACTAGTATCCAGGTTGCATGAGCCCCTGAT  
GCTTTCTGCTCGAGGGAAATTTGGAGCCATGGGGCAATGCCCCCTGACGT  
AACAGTCTCCACAGTTCTGCCATGTCTCATCCTGGCCCTGTAACTGGAC  
CCAAATCTGCTACCATCCCATCCATCTCAGGAAGTGAAACCTCTTATGTC  
AAATAGGTTGTGCAACGTATGTATCAGATCCTGTCTTCCAAGGAGACCG  
CTCAGGCCACAGCACTTCTTCCGATCCCCAATGAGCAGAAAATATCTCG  
CTATAAACATAGTTGGCACTAAGGAGGGAGTGGAAGAGTGATGATGATG  
TAGATGGTGTATGTAGCCCCAAGGAAGTGAACAAGCAGAGATGGGGAGCT  
GGAAAATGCCAGGATGCTCCAGCTTTTGGGGAATTATTAGCTCTTGAGTC  
ACTAAAAGCCTTCTCAGCTGCAAGTTCCTCTTTACCCTGTGAGGTCAATC  
TTCCAAGACAGGAGACTGACATTTATTCAAAGCAGCAAGTGCCCTGATAC  
CATCTTGTGTCTAATCATGGGCTTCGACGCCAGTTATCAAGGTTGATCTC  
ATCTCATTTGGTCTTCAATCATTTTGAACAAGAAGACAAGCAAAATAATCA

FIG. 4 (50 of 61)



TGGGTTAGTTCTTATATTATTGTGTGTACATGCAGTGATGTCTGTTCTTT  
GTAGTGAGCTGTTCCTTCCTTGTTCCACCTCTTGCTTAGAACAGAACTAA  
CAATCTGCCCCAACATTTTCCCCAATTTCCCATCTCATTCTTGGCACT  
GGCTGCTTAATATTTGTTCTTATGAGTCATTTTCTGTATCATTTCATG  
AGTCCCTCTGGGATCTTAAAGTATGAAAAATGTTGTGTGTACCCACACCT  
GTCTTTGTGGATATTTCTCTCCTTTCCCTTCTGCTTCTGGGATTATTTGG  
GAATGGGCACTATGATTTTTATCATATCGCTTCCACTTCCCTTATGGCAT  
CATCTCCAATGGGCTTCTTCTCCCTCTTGGATCCAGGTTCTCAGATTGGG  
GACATGCAGAGTCCAAGGAACATTCCATTCTCCTCCCTGGTCTAGAACAA  
GGAGGCTTAGATATATGAGCAGGTGGCTGGGGCTGGCGAGCTATGTAGT  
CTCCAATGATTTTTCCCTGATGTGCGAGTTGTTATGTCAGTTCTGGGAGA  
CCAATAAGACCTTGTCTTCTCCTTGGATCCATCAGAAAAAGCCCCTGGGT  
GGGTAAGATGGATGGCAGGGCTCTCCTACTCTATGTCTTTTCTCACACCT  
AGTGGGTATAAGAGAGGGGACCACAAACAGAGGGGGCTCTGGTACCACTT  
ATCCAGGGTCTGGAACATTTTCTGTAAAGGGCCAGATAATAAATGTTTC  
AGGTACAACACTCAACCTTGCATCATTTCAGAAAAGCAGTCAGATAATA  
CATAAATGAATGGGTGTGGCTGGACTTGTCTGCGGTCCCCTGTCTTATA  
TCATTGTATTATATCATTTTTTCTTACATACAAATTTAGAAGCAATACTT  
AAAAAAAAAAAAAGCCGTCTTTATTGAGCACCTACTAAGTGCCAGGTACCT  
TTTTTCCCTCATTATCTTATTAACCTCTTATAAATACCTTTAAAGTAGA  
TAATATTGAACCATTTGACCTATGCAGAACTGAGGTTGAGACAATAAAT  
TATTTAAGACCGCACAAACAGTAAATGCTGGAACACTACGACTCAAATATGG  
GTTAACTGAACCAAAACCAGATCTTTATTTCTCACTTTTAATTGTTACAT  
ATGTTTATTGCTCATCTCCTGTCCACATGGTGCCCATCGGCAGACTCCT  
TTCTCATTCTCAGTGATTGAGTGACATTCTAAACTACATTGGCCTGGCAG  
ATTACCTCTGTCCCTTAAATGTTTCCACATTGTCTTTTAGGATTGAGA  
TCTCTCTGTTCCTTGTCTTCCCTCCTTTCTTCTTCTGGCGGTGACGTG  
CTGTGTGAATTTGTTTCTTTCTCCTCTCAGGGTAGTACTGGGACTTTCCA  
AATCAGGGTTTTTAATGATCTCTCTTCTTCTTCTGAATTTCTTCTTAT  
TCCCATTCACTTTCTCATCTATAAGTGGCANCTTTGTTGCTGGAAGATAT  
CCCTTGTGCAGGGATTNCTCTTTAANAATTTGTCTNNNACC

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GTGATCGTCAACCTCCCACCCTGTAGGGCCTCAAGCATTGAGGACAATCA  
CTGGCTGCCCATTAACCCAGAAATGTTGCCGAGACAGGAGGCCGTGGCCC  
AAGTTCTGGAATGGGGTATTATTATGTGAGCACAAAGGCCTTTGCACAA  
ATGAAGGCTTTAAAAATGCAGTCTTAGTCAGGTGGAGGAGGGCTTATAGG  
ATTCCCAGGAATCTGGATCATTCTCTTGAGAGCTTTCCCTTGTCTCTGTT  
AAAACTCACATCGTACGGCCCAAATAACAACAAAAATGGATGTAAATTC  
TTGAATAAATCTGTGGATGGGGGAACAAGGCCACCCCCAGATCTGCCA  
GAAGCTTCAAGTGAGGGTCCCAAATGCCAAAAAGTCTGGTATCAGAGAGG  
ATGGCCAGTGACNTGGGGACACATGCCCTTTGCTGTGTCACTCAAGGAGC  
AGCAGCTTCGGCCCCGCACAGTGACCAGGACCCTGGCTTCCCACGCTGGG  
CAGGAGCTGGTGTCTGATGAAGGGAATGCCTGGCAGCACGTGCTGTCTGT  
CTCCTCGTGTGACCTTACCTGGCTTTGCTGCGAAGAGGCCACTTGCAATTT  
CTTTATTTTTTATATTTTTTTAATTTTTTTAAATTTTTTATTTTTTTA  
TTTTTATTTATTTATTTATTTTTTAAATTTTTTTTTTAAATTTATG  
CTTTAAGTTTTAGGGTACATGTGCACATTGTGCAGGTTAGTTACATACGC  
ATACATGCGCATGCTGGTGGCTGCACCCACTAACTCGTCATCTAGCAT  
TAGGTATATCTCCCAGGTTAATCCCTCCCCCCTCCCCCACCACCAAC  
AGTCCCCAGAATGTGATGTTCCCTTCTGTGTCCATGTGATCTCATTGA  
ATTTCTTTAAAGGTGGAATCTCTCAGTGGGGTCTAATCTGTTTCAAGAAAT  
TCAAAAGAGTATCCTTGGGAATGACTGGAATCCAGAGTCATCTGGTAAT  
CCTCATAAAACAACTCCTGGATGTCTCTCAGCACATCTCCACCTTGAAC  
GCAGGCTGGTTTCAATGGAGGAGCATCGCTCTACTGCACTTTTTTTTT  
TTTTTTGGCCTAAAGTGCAAAAGGGGATACGTTTCACTGTAAATAAATCAA  
CTGCAAAATCGTAGTTATGCTGAGCCCTGTCCCGTGTGTGGACACAAAG  
GAACCAAGGCTTTTCTCCCGCCCAACACACACATAACACACACACAAA  
ATCATAAAAAACATACATACCCCAACACATAACACACACACACACA  
CAAAATATATACACACACACACACCAAAACATGCCCAACAACTGTGTCC  
AAAAATAAATCCTACTGGTGGGTTTGTGGTCTCCCTAACTTCAAAATGA

AGCCGTGGACCTTCGCACTGAGTGTACAGCTCTTAAAGATGGCATGGAT  
CCAAAGAGTGAGCAGTAGCAACGTTTACTGTGAAGAGCAAAAGGACAAAG  
CTTCCACAACCCAGAAGGGGACCCAGCAGGGTTGCTGGTTGGGGTGGCC  
AGCTTTTACTTCCTTTTGGCCCCCTCCCATGTTCTGTTTCCATCCTATCAG  
AGTGCCCTTTTTCATCCTCCCTGTGATTGGCTACTTTTAGAATCCTGC  
TGATTGGTGCATTTTACAGAGTGCTGATTGGTGCCTTTTACAATCCCTT  
GTAAGACAGAAAAGTTCCCTGATTGGTGTGTTTACAATCCTCTTGTAAGA  
CAGAAAAGTTCCCCAAGTCCCCACTGGACCCAGGAAGTCCACCTGGCCTC  
ACCTTTCAACTCCATAATGGCATGAAAATACATATGTTGTACAAAACATA  
CATAACAAAGTATACATGCATCTCCCCAAATATACACATACCACAGAAA  
CATAACACAGGAAGTCAAGTACCTGTCAAAAGTCTGCATGGTATTGCC  
TCTGCAGTGAGTAGTTAGAAAAGTGAATTTGTTTTCAATAAATTGGAGT  
CCTTAAAAATCGTTGTAAGATAGAAAATTTTAAAGTATATAAAATAAA  
ATATGTATGTCTTTGGTCTAGCATTACACATGTAGGAATTTATCCTAG  
TGGAGTAATCAATGATATATGCAAAGATTTGGACAAGCATATTAAGCACA  
GAATTATGTATGCATATGTGTGTATATATATATATATCTGATACATAT  
AATAATGTAAAAGTGAATAAAGTCAAGTGTCAAAATTGAGGATTAGTT  
AGACTATGATCTGTCCATATGTGACATACAAGTTAGCTGCCCCCTTATTCT  
CTCGAGCTTCAACCTCCTATAAACAGTGTCCCTTGTATATCAGTATTGGT  
ACAGATAATCGAAGTTATTGAGGTTTTACATGGGGCAATAAAGGCAAGAG  
TTTATGAATACTCCATACTACACTAGGTAGCACCCCTATTAAAGACAAA  
CTCTTCTCTCTCATTTCCCTTCTTTCCGGAACCACTGGTTGAATCTCT  
ACAAGTCTCTATTGCAACTGCCTCAACATGGCACCCCTCCCTGCATCTCCA  
TCTTCCCTGTCTGAGAGCAATGGCCTGTGCCCCACACTCACATCCTC  
ATTCAATCCAGAAGTGAGCACCACAGAAAGTGCCTACAGTTACCCCAACCA  
CCTTCTTAGAAGATAAGTTAGTGTGTTTTGACTTTTAAAAATTTTAC  
TTCTCTTTTTCTTCAATCTCATCCCATCCCAAGAGGTTTATCAAGAA  
GTTCTCTAAAGATATGTGTCTCCTTATGGAATTTAACAGAAATCAGGGAT  
TTGTATTCTAGCCATCAAGGGAATAACATTTTCCAGGTCTTTAGACAAA  
TAATGGAATACCTTGCAAGTAAATTAGATACACTATTGTAGAAAAGTATTGA  
TGAAATGGAACGATGTTTGAAGATATCATATTGAGTAGAAAAGGCAAGATA  
CATTAAAGTAGGAAATGTATCTTACAAAATAATTTGTCAGACACACTCCTA  
TATTTGTATGTTATATAAATGCGTATGTGAAGAAAGGCTAGAGGATGAGA  
CCACAGTCTTCGGTGAAGTTTAAAGAGATGAGGCTGCAGCATGCTCAGAAA  
GGCCTGGGTTATAGTTCTTCCAGTAATTAAGGATGTGATCTTGGGTAAAT  
TGTCCATCCTCTCTAAACTGCACCACCTTTGTCTGTAAACAGGAAGGA  
TGGTATTTACCCCAAGGTCATCAAGGATTTGGTTGGAGAAAAATAAAT  
AAATGGGCTGAGCCAGACCTGGCACAGTGAGAGCACAGTGGTTGACTAT  
TGTGCTGGCCTGTTGTTCTGTGTTATTGACATGCTGCTGGTGGTGGTCC  
AGAAGCTATTACCTTAATTGGTTATGTGGATTCCCCTCATACTGAGCAG  
CTGTGTGTGGTGTGTAACCATAGCCATACACAGTAAGTGAAGGGCA  
AATGTGATGGAAGAAATGCAAGGAAGTGCAGATAAATAGCTAATGGGCTGT  
AGAAGGAAGCTAGTCTTGGAGGGCTTGATCAAGGAAGTCTTTTGCAT  
GTCACCTTTGAAGAAGAGGGGACATAGAAGAGGTATAGTGATCCCGGAG  
TGTACCTGGAAGGGAACATGAAAAGAGGACATTTTCTCTGGGACATGGG  
GACTCCACTTGCACTGAACTCTGGAATTGGGGCAAAGAACCATCATGAGAA  
CAAGGGCTTCTTGAACCTCCAGGCTCATTGGCTGATCTAAACCCTGTG  
TCCCCTCTTCTTCACTCTCCTCTGTTTTCTATACCTGTATTATTGGAC  
TGGACTGGAAGCCACCTGATCTATCACAAGTACCTTGAATGTGTTGAAT  
AGGTGTGGCACAGTCTTAGCAGAGTGGCACTACCCCAAGGAATTTGT  
TTATACCTTTGGCATGGAATAAGCAGGAATGAGTGATCACTGATAACT  
GAGGATGCTATTTATTATTGGCCAAAGGAATACTTGTGTTGATTTGCAT  
AACCCTCACAAGTCTGTTGATTACAAATGAGTACCAGACCTAGCTCCTTC  
AAGTAAAGGATCCTGAGAACTGAAGGCAACAGAGCTCCAGGAGTCCAAG  
ACAGAGCCACAGACCAGAGGATCCCTGGCCAGGTAGGTGGTCTCCTG  
CACTGGCTTTCAAGGCCAACAGGATGGATGGGGAAGTAGAGTAGCATCTG  
GCCATCTAGACCTTGTCTTTTATCCCCACTGGAAGCACATCTGAATTC  
TAAATATGATCTCTGAGACCTGCCAGAACACCTTGTCTCAGCCCCAGT  
AGCAGCCTGCTCTCTCCAGGAGGGCTTCACTAACAAAGTAGGGCATTGC  
TGGAGGGCCAGGCAGACACTAGCTTAGGAAATCCACCAACCCTGGAAATG

FIG. 4 (52 of 61)

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CTAGTCCCTTCTCTGAAGGCTCAGAAGACTGACTTTAGAGTCTAGAAAAT  
 ATTGGTCCCTTGGGAACAGATTTTGTGAGTGCAAAGAGATGGACTTCAGATGG  
 CCAGATGCCTGCTTCTTTAGGGAATTCTGTGAAAGCTCCCTGCATTTAT  
 CTTAATACAGGCAGCAGATTTTCATGAGTACCCCGAGGGATGGCCCCAGG  
 TCCTCCAGCCTGTGAGCATCCTTCTGTCTTTCAGCAGCACCACAGTATCT  
 TTATATGTCTTTGGATACCTACGTTTCTGCCAGACATCTCTTGCTCTGAT  
 GTCTGGCTGCCAAATTTCTGTCAAGCGCTCCAATTTTTGTGTCTT  
 TGATTTACCCCAACATGACAAAGGCAGTTGTGCTTCATGTATTCAGGGAT  
 ACTGCCAAACCACAAACAGGTTAAAAATCAAATAGCAGATATCCCTGTTCC  
 TAAAGACCCATCAGCTCTACCCACCTGCTCCTGCTCACCCTCCTTATTGT  
 TGAGTCCCTGAAGCCCTTCTTGTCTATTTTTATTTTTGTCATGAACAATTT  
 AGTTCCCTTGTCTCACTCCTAAACCTTTCTCAAAGGATTGGATTTGTAC  
 ACAAACCTGCTATCTCTGCAATCTTAGAAGTGATATGATTCTGAACAAAT  
 CACTTAACTTTTGATTTTTTATTGGTAAGATGGGAATACCAATTTTTGCT  
 CCATTTCTGCTATGTTGGCTGGGCTGATGTTGAAAGCTCTCGGTCAA  
 CTGAGATAGGGTGTGCAAAATTTATATATATAAATATATCTCTCCAACC  
 CCTCCCAATGAAGCAAGTCACGTGAGTCAATCCTACCCTAAGATATTAGG  
 GATTGAGCCTCCTGGGACATTTGGTGGCTTAGGTTTTCATGAAAAGAGGT  
 TGCAGAGCAACTGCTTTTTGTTAGGCAAAGATTAGGCTACTGCAGAGACT  
 CAGCAAACCTTCTATAGAGGTGTGAGATGGTAAGTATTTTAGGCTTTGCT  
 TGCCAGATGATCTCTCAACTAGTTAACCATGCTATTGTAGCCTCGAAGCA  
 GCCAGAGACAATATGTAACAAGAGCATGGCTGTGTTTCAATAAACTTT  
 ATTTAAAAAACAAGTCAGGGACCGGATTGGCCAAAGGCCATAGTGTGCC  
 AGCCCCAAGACTAGAGCAATGCATTTTAACTTTTTTATTTTTTGT  
 AAAATGCCAAGATCCACAAAAATGCTATTGCACCCCGTGTGTTAGCACTG  
 TGACTCAAGGTTTGGGAAATCTGCTTTGAAGGCGTGATAGACAGGAGAG  
 CATGGTCTGGCCCCCTTGGTGCCTTTCTGGTTGCAGCGAGCATTTCAAAC  
 ACAGAGCAAGGCCAGTGGTCTGTTGAGCACTAGAGACATGCAGCAAGGTG  
 TCCTGGGGTGAGAAGATGCCATAACTGGTCCCCCTTCTATCTCCTTAGGT  
 CTGGACTTCATTTTCTGTTGAGTAATAAACTCAACGTTGAAAAT  
 GTCCTTTGTGGGGGAGAACTCAGGAGTGAAAATGGGCTCTGAGGACTGGG  
 AAAAAGATGAACCCCAAGTGTCTGCTTAGAAGGTAAGGTTCTGTAGAAATC  
 TACCTCAGGGCCAAAGTGTAATTCCTAGAGCAGAACTTTGCTAGGTGCTG  
 TGACAGACCCAGTTGTTTCTGCTGACTTGCACAGTAAGTGAGCTTTCA  
 AATTTCCCTGGACAAATAACTAGACAAAGAGAAATCTGGAAGAGAAAAGG  
 AAGCTTTGCTCAGTGTCCAGGCACATCAGGTAGTAGATAAAAGGATCGT  
 CCTCAGCTTACAGATTTGGGGCTTTAGCATCCTGTTTGCCAACTGGATGGT  
 TGCATATGCTTCAAAATGCACCTCTTCCCTCCCAACATTCCCAAGTGGA  
 GAGAAGCTCCGATGAGAAGGAACTCTTAAGGCTGGGCTGAACAAATGA  
 CCCAGGCACAGGGCATCTGAGTATTCATGAGGAACACATTTGGGTGTTG  
 CCCATGGGGGACATAGGAGGAGGCTTTTGACCCAAATGATTGTCTACTG  
 AGGTGTGACGGGAGAGGCCTGTGACATGCCAGAGGCCAAACCCGTGATCC  
 AGTTCATCTCTATTCTATGTTTCTGAAGAGGGAAGCTATGATTTAATGTC  
 ATTACTATCATGCTGCTCTAGTATTTCTCAGCACATACAGAAGAGGGA  
 ATTAATGGTCTTGTATACCCCTAAATCCTTGGAAAATCCGAATTGCATA  
 TGCTAACCTCACTGCGTCTGACTGCAGACCCGGCTGTAAGCCCCCTGGAA  
 CCAGGCCCAAGCCTCCCCGCCATGAATTTTGTTCACACAAGTAAGGCCTC  
 GGGGTGAGGTGATGGGGGTGGCTGAGGTGCGAGGGTGGGGATGGGGGATG  
 GAGCCATTGGGTCTTCTACAGGGTGAGAGAATTGTAGAATGGGGACACC  
 TAAGGGTGCTGGATGGGGCTGAAGTCTTCTCTTGTGGAAGCAAATCCCA  
 TTAGGAGATAACTCTGGGAAAGATGAGCCCGGGAGGGGAGGTGATGCT  
 CACCTGCTAAGAGGCAAGGCAAGGAAGAGTTTGTGCTTGGGAACCTTC  
 CAGGTGCCTCTTCTGACCATAGCCAAAGAGACTGGAGACACAGACCTCCTC  
 CCAGCACTGAGGACAAACAGCCATGGGGCCAGTGGGGGTGCAGGGACACC  
 CACACCCTAAGGGCTCAGGGCGGCGCTTTCAGAGCCTGAACCTTCTCT  
 CATGCTGCCATTTGAACACCACAACACCCTAATAGGAACTGTTAACATT  
 GCCACTGTTGAGGTGTGGAAACCGAGACAGACAGTGGAGATTCCCTGCCC  
 TAGGTGACACAGGTAATAAGTGACAGATGTGGAAATTTAAAGGTACTATA  
 ACGTCTGTGCTGACTCAGGCTTAAGGCTCCCATCACCTCCTCTCTC  
 AGGACAGAGTCAGGAGGCCTCAGCCTGAGCCCCAGCTCTAGTGCAGGTTT

FIG. 4 (53 of 61)

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ATGTGGGAATACTGAGC FCACTAGTAL-ATGGCAGAGAGGACCAAATGG  
GACCAGGTGTGTAAGGGTGCCTGGCACAGTTGGGGGAGGCTGCTGTGCT  
TCTCCACCCGCTGCTGCTGCAGTTACCTTTGATGTTTTAGTTTTGTTGTAG  
TTACACCATTTGCTGGCTTTGGATCTGCACTGTGTCCACTCCAGGTGGAAC  
CAGGCACACAAGCCTCTCTGTGCGGCCTGTCTGACTTCTCCTTGTGAGG  
GCTGGGATCTCCTTCAAATCTGGCGGAAGTGGTTCTCCAAGTCTGGTCTT  
CAAACGTCAGCAGCATCAGCGCCTAGAAGTGTAGGAATACACATTCCCA  
GGCCCCACCACAGACCTCCTGCCTCAGAACTCAGGGCGCTGAGGCTCTA  
GGGGCTGCTTTAAACAAGCCTTCCAGGTTATCGTGACGCACCTTGAAAGTC  
TGAGAGCTACTGCCCTACAGAAAGTTACTAGTGCCCTAAAGCTGGCGCTG  
GCACTGATGTTACTGCTGCTGTTGGAGTACAACCTTCCCTATAGAAAACAA  
CTGCCAGCACCTTAAGACCACCTCACACCTTCAAGTGGCCTTGAGAAAGA  
TTTGGGGTCAAGGATCATGAGCGAGAACCACTTAAGAGGATAGTGAAC  
TAGTCTGCATGTGAGACGCTGAGATCCTATGTCAGGCTGTGATAGGAGGG  
AAACAGAAACCAAAGGAAAGAACAGCTTTAAGAAGCGCTTAAGAGGTACA  
AAGTAAAATGATGGTGTAGAAAAGTAGCTTCTTAAAAAGAGCATTTTCC  
AGTCTCACCCCTGGACTAACTGAATGAGAATCTCAGGAGTGTGAGGCCAG  
GTATCCATGGTCTTAAAAATGCCACCCACCAGGTGATCCCAAGTGTGCACC  
AGGGGTGAGAGTCACAGCCTTAGGCCATGCCACTCAAAGGGTGTCTTCAG  
ACCAGCAGCACCCACAGCTCTGGGAGTGCATCAGAAAGACAGAGGCTTGG  
CACCACCCACACCTACTGAACCATAGTTTGCAGGTGATTTCTTGCACATT  
AAAGTGTGGGAAATGGAAAAGCTTAGAGTTCAGCTAGCTCGGTGACTCTC  
AGTCAACCTGCACCTGCTCCATGAACCTCAGACTGCCTGGGATGGGCCAG  
AAAAGCTCCTGAGGAGATTCTGATGTAAGGCAGGGCTGATAACCATGGAT  
CTCATCTGACCCCATATCACTGGGGAGTTACTTAGGATCTTGCCTGGGGC  
CAGTCATCTCTCCATAGACACTGAGAGTGTCCACGATGCTTGGGGCACT  
ACAGGGTGGGAGGTGGAGGATCACGGGTGAGTCAGATAGGAAGCCTGCTC  
CTGGGGAGCTTACAGTGTCTATAGGGCAGCAAGCCAAGGATGCCAATACCT  
GTGTGCAGGTACCACTGACGAGTGCAGAGCGCTGCAGCACCAGAGAGGAA  
GCTACCCTGTGCAGAGGGGGCTGAGGAGGGCTGCAGGGAGATGACAGGAA  
AGCCGGTGTACAGGAGGAGTCTTCCCCACTCTTTGGGCATGAGGAGACC  
AGGAGGACATTCTACAGTGAGAAACCCAGGCAGAGGCCATGTGCTTATGG  
CATGGGAAAAGAATGACACCTTAGACTTATTCTCTACATTAGAATTGCCT  
ACCACAGATACCCATATTATAGCTTCACATAGTGTGGTGGTTACTGTGTT  
TTCATATTGTACATTTGCCATTTTCCAGCCACCCACCCATTCTTGACAG  
TCACTGGCCCCAGCCTGGGGGGCCCTGTTCTTTATCAAACAAGTGCCTGAG  
CTCTTTGCAGAGGTGAGGGTCACCTGTCCAATCAGAGGCCAGGAGGGAAC  
GTTCCCTTTAAGACCCTACTCTAGGCAGGCCTGGCCCAAATGAGTTGCT  
AGGAGCCCACGCCCTAAGAACCCTCTGAGCACTGTTGTGGCTGGTCCTGC  
TGCTAGAAAGTTGTTCCCTCCAGGGCCAGGTGCAAGATTTGTGGCTTTTCAA  
AGGAGCCACTAAAGCTCCAGCTCAGCCTTGCAAGGTGCTGGGCTCCTGGG  
GGCTTCTGCCTCCAACCCTCCCAACTCTTCCATCACCGCTCCCTTAGCC  
TGGCCAGTGCAGGGATCTGTTCCACTCTAGGCACTGCTGAGGGAATGATG  
CCTCCAGTCAGAGGGTGCAAAAAGAGAGTTAAGAAAAACAATGATTATA  
AAAAGTCTTTTTATACGCCAGACATTTTCTTGCTCAGGCTAAGTGCTA  
CTTATTTGAGTAAGCATTTTAGTTCTCATAACTCCTCTCTCAAGTAGGTG  
CTGCTATTACTTTTCAATTCACAGATGAGGACATTGAGGTTTGGAGAGACT  
TAGTAACTTGTCTCTGTCTACAGCAGAGCTGGGATTTGAATCTATCTG  
TCCAAATCTGGAACCCATTGCTTGACAGAAAGCTTAATTGCTTGTCCC  
AGCAAGATAGAAAGCCTGGGAGTGGAAAGAAATATTCAAGTGGCTGTGATGT  
CTGAGCCCCACAGGCAGGGTGGAGAGCTAGGGCTGGGGCCCTTGGACGTGG  
GGAAGAAAAGGGCTGAGTCTTCCATTTTCAATGTGAAGTGTGATATCTGG  
TGATATTGATCTAGGTCCAAAGGTGAAGAACTTAAACCCGAAGAAATTCA  
GCATTATGACCAGGATCACAAAGTACTGGTCTGGACTCTGGGAATCTC  
ATAGCAGTTCCAGATAAAAACCTACATACGCCAGGTGACTCTCAGTTTTG  
GCTGTGTTTTCTGCCTCCACCTAGCAGGGGTAAGGCCTCCTGCTAGGTGG  
GCTCAACTCCATGCTATACCATGCCCCATCTCCAGCAGGTGGTGAAGCG  
AGGAGGAGAGGGCCCGGAGTACTAGGGCATCAGATGAAGGGTCTCTAGCAA  
TGACCAGATCTGAAAGTAGTCTTTCTGGAAGGGCTGGAGAAAAAGAAGGA  
GGCAGACACTTAGACTGGAAGAAGAGGAGGCTTAAACCGGTGTGATGGAG

FIG. 4 (54 of 61)

GGAGAAGTGGACCACAGAGTCAAGGGAGAGGGACTGTGCATCAGGCCTGA  
AACCCACAGCAGACAGGAGAGACCTTCCCTGCTCTCAGAACCCACACATG  
TTCTGACTGTCTTTTTCCAGAGATCTTCTTTGCATTAGCCTCATCCTTGA  
GCTCAGCCTCTGCGGAGAAAGGAAGTCCGATTCTCCTGGGGGTCTCTAAA  
GGGGAGTTTTGTCTCTACTGTGACAAGGATAAAGGACAAAGTCATCCATC  
CCTTCAGCTGAAGGTGAGAGTTCTAGCTCAGTTTCTGGGCCTTTGGCTA  
CCCAAAGTAAAAGGCCAAGATCCTCAATGCCTCTCGCTTTCCTGCAAAT  
TCTTATCTTGGCCAATATAACAGGGACATCCACCTTCTGGAAGCACCAG  
GCAGAAGAGCCCCATAACTTCTTCTCTGGTTCTTGGCCCTTCTAGGGAA  
GGAGGAGAGACTCCTCACAGCGGGGAGACAGCAAGGAGCTGAGCACCTGT  
TCTCCTCTCCTGGGCTCACTGGTCTGGCCCTGGGCGGGTGGCGGTCCCC  
TCCTGCTGTGGCCCTCCATGTGGCAAGCAACACAATTGGGCCAGGACCTT  
GGCGTGCTGCTGTAGGGTAGGAGGGTGTGAGGGAGCACTCGGAGGGCAGT  
GTGTCTGCCCTGCAAATTTAGTCTGGATGGAGCATCCTTCACTTGAGG  
GGAGAAATCTTAGGAAGCTGAATTAGATACAGATCTAAGCCATATTCTCT  
AATTTTAAAAACTATAGAGCTGAGATTTTGGTATCCATCTGACTCTTACG  
TCTCTCTCTCTCTCTCTCTCTCTCAGTTTATTTTTAATCTGGGGGACA  
AGAAGGCCTGGAAAAGAGGGCATGATTGCTTATCATCCCTTAAATACCAG  
TACCAAGGCTGACACGTCACTTTCCCAAGGACCATCTGCCTTCTCTCTT  
TTCCTCCTCTCCTGTGTAAAGGCCTGGAGGATGAGCACATGTGCTGTGTT  
TTCCTCCTCTCAAAGCCTGTGCTATCTAATTAATCCCTTTTACCTCACA  
GAAGGAGAACTGATGAAGCTGGCTGCCCAAAGGAATCAGCACGCCGGC  
CCTTCATCTTTTATAGGGCTCAGGTGGGCTCCTGGAACATGCTGGAGTCG  
GCGGCTCACCCCGGATGGTTCTCTGCACCTCCTGCAATTGTAATGAGCC  
TGTTGGGGTGACAGATAAATTTGAGAACAGGAAACACATTGAATTTTCAT  
TTCAACCAAGTTTGCAAAGCTGAAATGAGCCCCAGTGAGGTGAGCGATTAG  
GAACTGCCCCATTGAACGCCTTCTCGCTAATTTGAACTAATTGTATAA  
AAACACCAAACCTGCTCACTAACTTTCTGTCAATTGGGTTTCAATTTCTCA  
TTCATGCTTTAAGGATTTGTGTTTTTAGGATATAGCAAGAAGCTTGTTTA  
ATTACAAAGTTCTGGGTTGGAAAGAGACCGGCTTCTGCTTGTGTACTGCT  
ACCCTGAACCATCAGACATGCATGTGTGTGTATGCTATGATGTGGCC  
AGTCTGAGTGCAATACTTGACGCGGAAGGAGCAGCTGGGTGCATGCTGT  
GCTCTAGAATTAGTCTTTCTACTGGGTTTGGTAGATTCTGAGGGCATT  
GATCCTGGGGCAGAAGTGGCTGAGTCTGTGTCTAGGGTACAGTGTGCAAG  
AAAGAAATGTAACAGCAAGTCACAATCCAGCCAAGTGATAGTGAAAAGG  
GGTAGTTAGGTCCCAGATAAGGAGCAGGGTGACTTGACCTGTGGGAAAGG  
CACAGAGACAAGGAATCTGGGTGAGATGACAGCCAGGAGACCAGGTGAGG  
GAGGAGCCAGGTACTGTCTGGGAGGCTTGTCAACAAGGGCATGGTCTTAT  
CACTAAGCAGGGCTCAGATCCTCATAATGGGGGAGTGAAGGCTGGCCGA  
ACAGAAATCAGGGCTGGAAACAGAGTGAGGGGTGGAGACAGGAGACTG  
AGGCTTGGAAATTAGTTTTATTAGTTTTAGCTCTTCAGTTACAAGCAATAA  
TAATAGCTTCTAGCTTATTTAAGCAACAAGTATACTACAAAAGGAGCTTT  
CTAGAAGGATATTGGGTATATTCAATTTCTTACTGCTGCTGTAAACAAATTA  
CCACCAACTTAGTGGTTTAAACAATGCAATGTATTATCTTGCAGTATATGG  
AGGTGAGTCTGGAATGTGTCTCACTGGGCCAAAATCAAAGTATCAGCAGG  
ATAGCATTGCTTTGGGAGGCTCTAGGGGAGAGTCAATTTCTTGCCTTTT  
CCAGCTTCCAGAGGCCACCTGCATTCTTGGCTAGTGGCCCACTCCCATC  
TTCGCTGCTTGGGTTTTTCTCACTGCTTTGCTCTGACCTCCTGCCTT  
CCTCTTTCACATATAAGAACGCTTGCAATTTACATCGGGCTCACGTCAAT  
ATCCAGGATACTCTCCGTCTCAAAGAGGCTTAACTTTAATCACAGATGC  
AAAGTCCCTTTTGCTATGTATGTAACATATACAGGGTCTGGGGATTA  
GAATGTGGACATTTTCGGGGTGCCATTATTCTGCCTATCATGTGAAGTAA  
CTTTCAAATGGAAGACATGCTGAAGAAAAGTCAAGGATTTCTGGCAG  
GCCAGAAATGACAGAAGGCAGAAAACGTTGGTCCCATCACTCAGATGGGT  
AAGAGCCAATCAGTCTTTTGTGCAAGTGAAGAAAGATTGAGATTCCAAGC  
AAAGCATGCAACTGCCCTAGTTTGGGTGATGTGTGCACTCCTTGGTCAGT  
GAAGGGCAGCACACCTTGATCAATACTCCCTCCAAGACTGTATCCAACGA  
GGCCAGTGATGTTCTCAAAGCAGAGCTAGAGAGCTAATCCAGGAGAGA  
GGCGTGTGGGTGGTGGGCAGGAAGACAAAGCTCAGCCGTAAAGGAGTAGT  
AGGGACAGCACCTAGGCATGGAGGCTCAAGTGAGATGATACCCATGGGA

FIG. 4 (55 of 61)

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AAAGCTCTGATAAGGTCAGCTCCTTCTGTTTCTGATCCTGATGGTGATG  
TGATCAACACCAGCCCAGTGACAAAAAGTACATAGTATATTTAGTAGAT  
GTTTCCACACAGAGAAATGGTAAATATTCAAGGCGAGGAATACTCCAAA  
CATCCTACCTTGATCATTACACATTCCGTGCATGTAATGAGTACTTGCAT  
GTATGCCATAAATATGTGAAATATTATGTATCACTATATAAAAGAAAAA  
AAATGTGGCCAGGTGACATCCATATTTTGGAGAGGAAGGCATGTCTTCTT  
CATTAATATCACAAAACATTTTCCACAACAAAGACACAGCTGTTCAAATTA  
GTCTCTGAGCCGGGGCTGTCTCATGGCAGTGAGGACTCTGGTTCCCTTAC  
AGACTAGCAGAAAGGAGATGGGGCTTACTGACCATGGCCTTGAGGAGGCT  
GAACATGCAGGCCAAATGGAGACACAGACAGCCTGGGCTTGGTCTTGCTC  
CATCCCCTTCCAACCTGATGAGATATAGTGAGTCACTATGACGTGGGTCA  
CTCATGCTTCTGTGAGGCTCCACCAAGACAGCAAGTGCATCAACACCTT  
ACGGAAGCACAAGGCCCTGTTTGTGTTGACTTCATGAAAGGCATGGTTG  
TGGTGATCGCATTGAGTAGGCTTTTGGGTGAGAGGTGAAAAACCCCACT  
ATCATGCATTGCAGCCCTCTGGTGGAACTGTGCTTCAGGCTCTAAATTT  
CAGGCTCTAGACTGACTCCAGGATGAGTATTTGGAAGCTGAASTCAATCT  
GTGGTCTCTTCTCCTGTAGAGCAGGAGTCAGCACTTTTCATAGAGTGCCA  
GATTCTATATATCCTGCCACATGCTCTGTTGTACAGAACAAAGAAGGCC  
ATAGACAGCATGGCTGTGTTGGCAAATACAAAAACAGGCAATAAGCTGT  
ATTTGGCCTTTAGGCTGCAGTTTGCCAACCCCTGCACTAACACAGAGCTT  
AAAGGTGGTGGTGGTGTGCTGGAGCTAGCTTATATCAGCTTGCAATAGCC  
AATTGCTAACATCTCTTCCAACTCTGTGCTGTGCTTGTGCTTGTGATAG  
TTTGAAATTGGCTACCCCATTTAATGCTGCAATCTTTTCTCACCCAGCA  
CTACTGACTCCCTTTGCCCTGTCTTATTTTTCTCACTCTAACATGCTGT  
ATAGTTTTCTTCTTACATTTATGTTTGTGCTTCCACTAGCATGTATGT  
CCCACAAGTTCTTTGCTCTGTGATGTATCCCAAGAACCCACTGCAGTGCT  
TGGCACTTGTAGGAACTCCATAAGATTTTTATAAATGAAGAAAGGAAGAA  
AAAAGAGAGGGAGGGAAAAAGGAAGGAGCCTTCTATTTAAATGATGGC  
CTTCTCCATATTTCTATAGTAATATGACTTCCCTTGCAAAGGGGGATGCA  
TTTTGGAAATTTCTATAAATAAACTCAGGTGGTTTTGAATTTCATTTTT  
CTAACTGTAATTGTAATCATTGGTCTTTATGTTTAGTGAAAAAGTTTTGG  
CCCTTATGCCTCACACCTGAGAATCCCAAAGTATTGGTTTGTAGAGCTC  
CCATAGAGAACCATAAACTGGGTGGCTTAAAAACAAGAAATGTATCGTC  
TCCTGGTTCCAGGAGGCCAAAGTCTGAACTCCAGGTGTTGGTTCATTCTGA  
GAGCTCTGAGAGAGAATCTGTTCCAGGCTTCCCTTCAGTTGTGGTAGCT  
CCAGGGTCTCTGGCTGGTGGCAGCAAACTCCAGTCTCTGCCCCCATCT  
TCACATGACTGTCTTCTCTGTGTTTCTGTGTCCAGATTGTCTATAAG  
GACAGAGTCATACTGAATTAGGGCTCACTCGAATGACTTCATCTTAAGT  
GAACTGTATCTGTAAAGACCTTATTTCCAAGTAAGGTCAATTCACAGCT  
ACTGGGGGATAGGACCTCAACATATCTTTTGGGGGACATAATTCAACTC  
ATAATACCCAACATGATAACTGTTTCATCCCATGAAATTTAATGTCTCTCA  
AAAGGTGATCTCAGGGCATTAACTCTGTGACAGAACTCCCATAGGAAAC  
ATTCCAACCAGAAGCTCCTTTCACAGCTGGTCACTCCTCCTACCCCATCC  
GAGGTCTGGGGCAGGGTGAGGCAGGTGGGGACAAGAAGAAGGCTGTCTC  
GGGTGTAGAAAAGAGAAGACCTTATTCACCCGGCACTCTGTTTCATGAATG  
AGCTATCCAGCATAGGATATAATAAATCGCTTTAGGAGTGGTAGACTCCA  
AACATTTTTTTGGTCCCAGTTATCCTAATCAATTAACAAACTCTAGAAC  
CCATCTTGAAGTGACGGCATTGGGACATTATGAACTTACACAGAATTCA  
AAAAATTTACAAGGGCTAAATAAAACAGGGTCTGACATCTAATATTTTCTT  
CCCACATTCCTATGCATGTCTGGCTCAACCATCCCCAACCCCTCACTCTC  
ATCCTGGTGGACACATGCCTAGTGATGTGATCAGCTGGTTACAGGGGGC  
TGGTGATGGTGGATATACAGCTTTTGGCAATTTCCATGGCATAACTACTC  
CAAATATGGCCAATTTCAAACCTACCAACATGAAGGCACAGACACAGAGTT  
TGGAAGAGATGTTAGCAATTGGCTATTGCAAGCTGATATAAGCTAGCTCC  
AGCACAGCACCACCGCTACCTTTAAGCTCCTTGTGTTAGTGCAAGGGTTG  
GCAAACTGCAGCCTAAAGGCCAAATACAGCTTACTGCCTGTTTGTGTAT  
TTGCCAACACAGCCATGCTGTCTATGGCCTTCTTGTCTGTAAACACAG  
AGCATGTGGCAGGATATATAGAATCTGGCAGTCTTAATAAGTGCTGACT  
CCTGCTCTACAGGAGAACACAGATTGTCTTCAGCTTCCAAACATTCTCT  
CTGAGTCAGTCTAGAGCCTGAAATTTAGACTGAAGCACAGTTTCCACCAG

FIG. 4 (56 of 61)

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AGGGCTGCAATGCATGAAAGTTGGGGTTTTACCTCTCACCCAAAAGCCT  
ACTCAATTTTTTACTGCAAAAACATGTTATCATCATTATTTTTTACTTAG  
CCCACCTTTCTTGGCAATTTTCCATAGGAAAATGCATTCTAAATTTCAA  
CTAATCAGGGGACTTGGAGCCTCTGGACACCCCTTGTTCCTTGCCACA  
GTCCCTTGCAAGAGGTGCCTTATCAGAGCGGCTCCATGCAGGGGCTCAGG  
ACAGGATCAGATGTCAGTTGCACCAAGGGGGCAGGGACAGATCCTCTCTG  
CTEACCATGCAGAAAGGACTGTTCACTGCACCGTCATGGTCTGGTGATT  
TCTGGTCCATAAGGGAAATTTTACATGCATCGGGTGATTGTACATCAGC  
ACAACACTGTGAGGAAGGCAGAGTGAGAATTTGTGTGCCATTTTATAGG  
TGAGAAAACAGATGCAGAGACATTAAGTAACTTCACCACAGTCATGCGGG  
TTTTAAGTGGCAGACTTTAGGTGTGTGACTCCTAGTCCAGAGTTCTTT  
GCACTGCCCTGAGGTGCTAAAACTCTACTGTGCTTTAAGACTCACTTGG  
GGAGCTTCTTAAAGAGAGATTGCACAACCTGAGATTCTTGTTTAACTG  
TTTTGGGATGTAGCTCAGGGATCTAGCTGCCTTAAAAAAAACCTCCA  
AGTAATCTGATGCAAGCGGTTCTTTTTTGTCCACCTTTGAAGAAACACT  
GCCTCCTCCCATACATTTTCAATTAGAAAATGGTAACATGTTTTCAGCCT  
GAGAGCCATTTCTGGGTGACCGGACGTCCGGCAGCCGCTGTACTAGCTTT  
CAGTCTAGGCTTAAACACACATGATAGGAGATGTCCTACTCCAGATGATA  
TGAGTCTGAACCATGGAAAAATTCATTGTGTGGCACATCTGGTGGGTGT  
GCACTGTCCCCAGCAGTGAGGCACCCAGTGAAGACAGCAGCTGGGAGAGG  
CTTAGTTACATGCAGTGGGACAGTGTGGGCTAGACTGCTGAGCCCTCTGC  
AGTTTACTCTGTGTGAGGCAATGAGGGTGAAAGGCTGATCAGACCCACGT  
GCAGACCATACCTCCAGGGAGACAGATATCAGTCAGGACAACCCCAAGT  
GTAGCTGGAGAAGCAGTGCCAGGTATGACCGGATGTGTATCCAACCAGG  
AAATCTGCATATAAATATAAGAGGAGAAAATGAACAGATGTTGCTCTTAT  
ATGTAGATATTTATGAAGAGCATATAATTTTGTGTGTGTTTAAGAA  
GTTTATAAGTATGCCTTAAAAATGTATAGTATATACTGTAGGTATTTTTT  
CCATTAGATATTTGTGTCTTACTTATCCACATTGACATTGTAGCAAC  
AGTATAATATAACAACCTCCTCTACAAAAGCAGAAGGAAGTGAAGCTTTG  
GAAGGAAGCACCCAGTGAGCTTGCCCTTTAGGTGGGTGAGTGAAGCAG  
GAGTCAGTGAGGTTGAGATCCTTTGAGAGGAGGCAATCATTAAACCAGGAA  
ATCTGCACTGCATCCTGGCCACACCTAACCTTGGACAATGGTGTGTTGGA  
GCGCCTTCCAGCTCTTAAGGCTTGCGATTTCTTTCTCTCACTCTTCAACC  
ACGATGATTAAATCTTCTCCTACAGAGTTGGACAATAAAGCCTTGAGTTC  
CTGCCTCCCTGGTGTGATCAGGAGCATAGACATGGCCAGGAACATGTA  
GGTGTCTTTGAAAGCTGAACAAGTTAGTAAATTTCAAACCTCATTTCACC  
CACCAGTAAATGGGAATAATAAACCCTATTTTACATAGGGTTGACAA  
GAGGAGTAAAGAGGGATTCAATGAAAGTTCGTTATTATCATTGTAGTAG  
CAGTGTGATAATATCAACTGAAAGTTCATTATCATTATTAGTAGCAGTA  
TTGATAACCTCTTTCTGTGCCTTCTCACTGGTGGGCCCAGGCCATCAG  
CAATGCCCAGGGTGTCTGGATCTCTGCTGCATCGGGCACCAGCTGTGTC  
AATGGTGAGAACAGTACAAGGGTGGGCAGGGCAAGGCAGGAAGCACCCAG  
GAGCAGCAGCTTCATGGGGTGAAGATGTCAGGAGCTTAGGGACAGTCAGA  
GCGGGTGTGCCTCCTCTTGTGGAGCCTTTCTGCTGGGTAGGAAGTGTG  
CAGCTGTGGCCATGGATTACCTGAATATGGGTGGAATTAGGCATTACAGC  
TGGGTTAGCTGTGCCTAGAAGGAGGAACTCTAACTGAGAACTTGTCCCT  
ATTGCCACCTCTGATAGGCAGATGATCCATCCATCAGTGGCTGAGCTGAG  
GTGTGCATGGGGATGGGTAAGAGCCACACACAGGGCTGATGACTGAGTC  
TATTTAGAACAATAGATGTAAATCTGATAATGTAAATGTGATAGATTA  
TTTTGTCAATTAGAAATGGTACCATATAATTATATATACATAAACATG  
TATACATATACACACATATACATGTGTGTATAAACACACACAGTATTGTC  
CCCTACTCATTCCATAAACCTGATGCCTTTAGCTGGGATTCCCAGCTTTC  
ACTCTCCTCTGTCTATCTGTCTATATCCTCCCATCCTGTAATTCT  
GGCTTATATGCCACTTCCCTAAAGCCCTCCCTCAATCCCTTGCTGGA  
AGTGACATTTTCTCTTTGAGCTGCCCCTGCTTGTGCTTTGGTGAGGTCA  
GCTGTATTGCAGTACCTTGTATTGTGGTTGTACATCATCGTATAGAATT  
AATTTCTGACACATTCCGTATTTTTCAAAGGGCCTAGTGTGGGGCTTTAA  
CAGTAACACGCCACCGCCAGTTAATTTTTGTATTTTTGGTGGAGA  
CAAGGTTTACCATGTTGGCCGGGCTGGTTTGAAGCTCCTGACTTCAGGT  
GATCTGTCTGCCTCAGCCTCCTGGAGTGCTAGGATTGCAGGCATGAGCCA

FIG. 4 (57 of 61)

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CTGCACCCAGCCACCTATCAAAAATTTTAAGTGCCATTTTATTTTTTATT  
TTTTGTAGAAATGGACAAGCTGATCGCAAAATTCACATGGAATTGCAGGA  
GGTTCCAAATAGCCAAAACAATCTTGAAAAAGAAGACAAAGTTGGAGGA  
TTTACACTTTCCAGTTTCAAGACTTAGCTCTTAGCTACAAAGCTACAGTA  
ATCAGAACACTATGGTCTTGGCATAAGTGATGCTGGACAGGTGAGCCCCA  
AAGTGGGACTTAACCTGTGAAGGTTCTTGGCCTTGCCAGGAAGGAATTC  
AAGGGCAAGCCAATGGGACAAGAAAACAGCTTTATTGAAGGGGCAGTATT  
ACAGCTCCAGCCCTGTTACAGCTCCAGCCCTGTTACAACCTCTGACTACTC  
CTGCACAGAAGGGCTACCCTGTAGGCAGAGAGTAGCAACTCAGGGCAGTT  
TTGCAGTCATTTATATCCACTTTTAACACATGCAGATTAAGGGACAATTT  
ATGCAGAAATTTCTACGGAATTGGTAATAACTTTTGGGTCTAGGAGTCAT  
CATGGAAGGGGGGGCGGGGAACCTCCCTGGTGTGCCATGATGACGGTAAAC  
TGATATGGCGAAGTGGTGGGTATGTCACATGAAAAGCTCCTTCCACCCCA  
GCCCTGTTTCAATTAGTCTCGGTTTGGTCCAGTGTCCAAGTCTGCCTC  
CAGAGTCAAGTCCCACCCCTACCTCTTAAGGAGAGATGTAAATACATGG  
AATAGAATTGAGAGTCCAGAAATAATCTCATACATCTATGATCAATTGAT  
TTTCAGCAAAAGGTGCCAAGACCATTCAATGAGGGAAAGAATCATATTTT  
TTCAACAAATGGTGTGGATAACCACATGTGAAAGAATGCAACTGGGCCC  
TTATCTCACCCATATACAGAAATTAACCTCAAAATGGCTCAAACACTTAC  
ATGTAAGAGCTAAAACCTATAATATTCTTAGAAGAAAAACAGGATATATCT  
TTATGACCTTGGATTTGCTGGCTGATTCTTAAATGACACTGAAAGCACA  
GCAACAAAAGAAAAAAATAGGTAAATTGGACCTCATCAAAATTTAAAA  
CTTTTATGCTGGGTGCACACCTGTAATCCAGCACTTTGGGAGGCTGAGG  
CAGGAGGATCTCTTGAGCCCCAAGAAGCTGAGGCTACAGTGAGCCGAAT  
GTGCCACTGCACTCCAGCCTGGGTGACAGAGCAAGACCCTGTCTCGAATA  
AATAAATAACAAATATATAATTATAGATCTCTGGATCTTGCCTTCGGAG  
ACTGACTCAACTAACTGGTCTGGGTGGGAGCCAGCCATTTGTATTTTT  
GAAAACCTCTCAAATGATTTTACTGTGCAGCCAAGGTTGAGAATCACTGT  
ATCATAGGGTTGGACTCCTAACTGGAAACAGTTTGCACCATCAGGTGTCTG  
CAGCATTCTGATAATAGTTAAGCTTTTCTCTAGATTTTCTGATATTAGA  
TGAGTCATGTTTACAAGTTTTTACCAAGAGACAACTATCTTTCTGCCCT  
TACTTTCTCTCTTATACTATTCTAATCCAGAACCCTTTGGAACCTCCAC  
TGAGAGATGAATCTAGAAAGTGACTCTCTTGGCTACAACAGAGAGTAATG  
TTGGCCTGTTTGTGCCAGATCCAGTTGGTGTGGTGGTGGGACAGCACCT  
CCCTGAAATCCCCTCCTCTCCCGTCAGATTCACTCCCCCATTTGCATCAC  
GTACAATCATCACTATGGGTTTCTATTACCTTGCTAGGGCATTGAGAGT  
ACCATATATACCAACTATTAGTTTGGAGCCATGGTTCCCAAAGTGTGGAC  
TGAGGGCACCTCAGCACCTCAGGAGGTGTCTGGGATATTTAAATATT  
CTGAAGAAAAACACAGTGACATCTGTGAGGCCGTGAAACCGTTGGCATT  
AAATTGTCTCAACCCCAATTGCTTAAGAAGCAGAACTGGCCAGGCACGGTG  
GCTCACATCTGTAATCCAGCACTTTGGGAGGCCGAGGCGGGCAGATCAC  
GAGGTGAGGAGTTCAGAGACCAGCCTGACCAACATAGTGAAACCCCGTCTC  
TACTAAAAATATAAAATTTAGCCATGCATGGTGGCATGCACCTGTAACCC  
CAGCTACTCAGGAGGCTGAGGCAGGAGAATTGCTTGAACCTGGGAAGCGG  
AGGTTGTAGTGAGCCAAAATCGTGCCACTGCACTCCAGCTTGGGTGATAG  
TGAGACTACATCTCAAAAAAATAAATGAGAGAGAGAGAGAAGCAGA  
ACCATCAGGTGTTTCTTTTGGCTTAAAGTACTCTGTGAAGAAATTCCTGG  
GACACGAAGGATACCATGAACCTGAGAGATTTTGGGAACCTCTGCTTTAGA  
AGCTGGAGGTAGCATTCTTGGGCACAGTACTGCCTTGGGATCAGCAAAT  
CCTTTTGTAGGTGCATTAGGTGTGGCAAGACAGCTCTTAGAGTGGGACC  
GGGATGTGCTTGGAGACAGAGGGAACCTAGATTGAGCTGCCCGATAAAGAC  
ATGCCAGCCTGGCAGAGTGTAGTACTCATGTCTGTAATCCTAGTGCTTT  
GGGAGGCTGAAGTGGGAGGATGCTTGGAGGCCAGGGGTTTGGATCAGCC  
TGGGAAACAACAAGACCTCTACAAAAAAGAAAAAATAAACC  
CATGTGGTGGCATGCACCTGTAGTCCCAGCTACCTGGCAGGCTGAGGTAG  
GAGGATCACTTGAAGCCAGGAAGGTAAGGATACATTGAGCCATGACTGTG  
CCACTGCACTCTAGCCTGGGTGACAGAAAGAGACTCTGTCTCAGAAATAA  
ATTAATAATAATAATAATATATAGTGGCCATGACATCCCTAGAAAGACA  
AGGTCCTGGGAATAGGTAGAAGCCAAGGGAATGAGAAATGAGAGGGGGC  
CCTGGAGCTGGAACCTGGGGGAGCAGGATGGCCTCTGAGAAGTCTTGATA

FIG. 4 (58 of 61)

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GTGGTGTCACTGATGTGTCTGATGTTTGTAGTTGTAATTATTTGCTGGGCCC  
CTGTGATCCCTCATATCTGATAGCTCTTTGCTAGTCAAAGTGTGGTCTGG  
GGATCAGCGGCATCAGCATCACTTGAGAACTTGTTAGAGATGCAGAATCT  
AGAGCCCCACCCGGGACCCAGAAACAGAGCCTGCATTTTAAACAAGCTCCC  
CAGGTGATTCTCACACACTCGCATTTGAGAAGCACTGGGCTAGTTGAC  
AGATTCTCAGGCATGGCTGACATTGAAATATCCAGGGAGCAGGCTTGGCA  
TTAGGATGTTTTAAAGTCTCCAGGTGTTTCTAAAGCCAGGTTTGAGGAA  
TTACTGGGCTGATACAAATGTTTTGTGATGATGCTTTGTGTGTGTGTGTG  
TG  
TGGGTCACTTGGCACCAACACAGGAAACAATGGAAATATGTGAGCCATGA  
CAGAAAGGTCAGGAGATAAAAGAAATTAGTGACATGAGAGGTACTCCTCA  
GGTGTAGGAAAGAGGGTAGAGCAAACCAGGTTTTCCACCATATGTTGGA  
TAGGGGGTCAAGTAAATTTCTACTTAAAAATTACAAACAGGGGGCTGGGCG  
CGGTGGCTCATGCCTGTAATCCCGCACTTTGGGAGGCTGAGGAGGGCGGA  
TCACAAGGTCAAGAGATTGAGACCATCCTGGCCAACACGGTGAAACCGTG  
TCTCCACTAAAAATACAAAAATTAGCTGGGCATGGTGGTGCCTGCTTTA  
TTCCCAGCTACTCGGGAGGCTGAGGCAGGAGAATCGCTTGAACCTGGGAG  
GTGGAGGTTGCAGTGGGCGGAGATCGCACCCTGCAATCCAGAGCGAGAC  
TGTGTCAAAAAAAAAAAAAAAAAAGAAAAATTCAAACAGGATGACCCTAAG  
CCTGCAGGACTTGGAGACATCTAGGTGACTGATACTCAGTCACAAAACAT  
AATTGGTCAAGGCCTGATGAAATGCACAGCAGACCTTCAGATGGTATGC  
ACTCAAGTGATATCCACAAGTCCACCTAAAGAAATGCTATATTGAGACAT  
TTGGCATCAATCTCTATCAAAACAAAGATAGTCCAAAGCAATGGGTTCAC  
AAACACTTTCTAAGACAAATTCTCTATTTGCTTTTAAATATCAGTCATCC  
CAGCCCTTGAATAGAGGAGCAAATGATACCAGTGGTACCCCTACCACAAT  
GCACCAAGGTATTATACTCTCATGCTCCATTTTCTCCCTCTGTCTACATC  
ACTAATAACTCATTGATTTCTGGTGCAAGCCCTGCTGGGAGAAAAAGTCT  
ACTCTGTACCTTGGAGCAAGTTGCTCAGAGTAGGTATCGAGGATAAAAT  
TTGGAAAGTTAGAAAAGCTATTAGAAGGAGATCCTAGTAGTTGAAAACAC  
AGCCTGGCCAAGTCAATGATGCTATTTCTCTCCCCAGCCTTGCATGTCC  
ATAGCTAAGGAAGACAATTTAGGCTTGGGCTAGAGGATGGGAAAGGGCAA  
AATTACTGATGCCACAGCCCAGAGAGGTATTCTAGTAATCTGAGGGTGAG  
GACCACATACCTGGTTCAGGGACGTACAGTGTGACAGCTGTGAGTGGAT  
GCCTGGAGTTCTGGCGTGTCTTCTAGCACAATGATACCTGAGACTCTTGC  
ATCATTGGGAATAATAAAATGGGAGTGGATAGATATGAAATTATGATGGC  
AATAAGCAATCAGCTAATAGCTTCATTGATGGGACAGATTAAAGATGGCT  
GCAAAATCCTTTGGTCCAGGTTTGGGATATAGGCAGCATTTGTATTGGAAT  
GCTGATAGTCTGAGGCCATGAAAAGTCCACCTGCAGTAGTGGTAGGAGGA  
ACAAGCCTCACTTTCTTCAATGTGTGTGACTGCTGTCTTGATTCCCTGGG  
TGGCCAGTTCATTTCGTGTGGTCTTTGGTCCACTTGACTCTGGGGTGGC  
TCTGTGATGGCTTGACCAATACAAATGTAGTGGAAATGATGCTGTCTCAT  
TTCCAGCCTCTTCCAGCCTTAAGGAAGTGGCACTTTTATTTCTGTCCCT  
TGGAATACTTGTCTTGCAACCCATCCATCATACAGTGAGAAATTCTAAG  
CTGCCCCATTAAAGAGGCCACATGGTGATAAATTGGGGTCTTACATACAG  
CCCTAGCTGTGCTCCTAGCTGACAAACAGTAGCAACTTGTCAACAGGCGA  
GTGAACCACTTAGGACTGTATACTCCAGCCCCAGTTGAGCAATGTGGAAC  
AGAGTAAACCATCTCAGCTTAGCCCTGCCCAAAGTGCAGAAATTATGAGCA  
AAATAATCCCCTAGGCTTTGGGCTGATTTGTTCCAGATTACTGGAACAGA  
ATTTGGTACCAGGGGTGAGGTGCTACAGCAATGAAAGCTTAAGACACGTG  
ACTTTGGTTTTGGGTCTGAGTGGCAGGGGAACTTGGCAGGCCTCAAGGAA  
ACTTTTAGGGAGGGTTGAAGCATAGTAGGAAAACAGTAGGGGAAGCTAG  
AGGAAAAAATGATGCTTGGTATGTAGTGGTGGGAAGTTTAGCAAACTCG  
CCTGATGTAATGTGGGAAATTTGAAGAACTCAGAACGATTTAAGGGCATG  
TTTTATAGGTCTTTAAGAACTTCTAGGCCAGGCGCAGTGGCTCATGTC  
TGTAATCCCAGCACTTTGGGAGGCTGAGGTGGGCGGATCACAAGGTCAGG  
AGATCGAGACAATCTTGGCTAACATTGTGAAACCCCGTCTCTACTAAAAAC  
TACAAAAAATAATTAGCCGGGCATGGTGGCGGGTGCCTGTAGTCCCAGCT  
ACTAGGGAGGCTGAGGCAGAAGATGGCGTGAACCTGGGATGTGGATCTT  
GAAGTGAGCCCAGATTGTGCCACTGCACTCCAGCCTGGGCAACAGAGTGA  
GACTCCGTCTCAAACCGAAAAAAGAACTTCTAGGGC

FIG. 4 (59 of 61)

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TGGTCCCCTGGAAGCCTCACACATGGTACACAAAGGCTGTCTTGAAAAGA  
AACGTAAGTGTGTTTTTGGTTTAATAAAATTGATTATAAATGGATAATG  
CAAAACATTTTAAAGAATTTTACTAGCTTACATTAGCAGATTTGGATCCA  
GTGATTGTTACATTCTGGTACTGAGCCCCTGAATTACTTCTTTGAGTAAG  
GCATTATACCAAAGCTATTGATAGTTGGGCTTATAGGGTGTATGTTTGAA  
GAACTACTAATGTCAAAACCAATATTTACGGTTCGACAAGAGGACATCAG  
AACTGGTAATCCTTATTACCATGACTGGCTGGACAGAATACTCAATGTAA  
TGGGATTTCTGCAAATAAAGACGGGAAGATGTAAAAAAGATGCCTGAA  
CATTCAACATTAATGAAAGATTTGAGAAGAAATATGTATACTAACTGCAG  
CCTTATCAAGTATATGGAAAAACACAAAGTTAAACCAGATAGTAAAGCAT  
TCCACTTGCTTCAGAAGTTTCTTACTATGGACCCAATAAAGTGAATTACC  
TGAGAACGGGGTCCCTGTTTCTCGAAGACCCACTTCCTACATCAGACGT  
TTTCAACAGTTGTCAAATCCCCTACCCAAAATGAGAATTTTTAACAGAAG  
AAGAACCTGATGACAAAGGAGCCAAAAAGAACCACCACCGGCAGCAGGGC  
CATAACCACACGAATGGAAGTGGCCACCCAGGAATCAAGACAACGGTCAC  
ACACAGGGACCCCCGTTGAAGAAAGTGAGGCTTGTTCCTCCTACCACTAC  
CTCAGGTGGACTTTTACGGCCTCAGACTATCCGCGTTCCAATCCACATG  
CTGCCATATATCCCAACCCTGGACCAAGCACATCCAGCCGAAGAGCAGTG  
TAGGATACTCAGCTACCTCCAGCAGGCTCCACAGGACCCACGTGAGACA  
CACGGGTACTGAGCTGCATCGGAATCTTGTCCGTGCACTGTTGTGAATGC  
TGCAGGGCTGACTGTGCAGCTCTCCGTGGGAACCTGGTATGGGCCATGAG  
AATGTACTGTACAACCACACCTGCCCAGTAGCCAAGTTCCTTCCACCGCT  
TTTCACAGATCGGGGTAGTGGCTTCCAGTTTGTACCTATTTGGAGTTAG  
ACCTGAAAAGAAAGCGCTAGCACAGTTTGTGTTGTGATTTGCTACTTTC  
ATAGTTAACTTGACCTGGCTCAGACTGACCAGTACTTTTTTCCGTGAC  
AGTCTATAGCAGTTGAAGCTGAGAATGTGCTAGGGGCAAGCGTTTGTCTT  
CATATGTCATGAATTCCTCCAGTGTAACAACATTATCTGACCAATAGTAC  
ACACACAGACACAAGGTTTAACTGGTACTTGAAAACATACAGTAGGTGTT  
AACTCAGTGAAATAACCAGGACTCAAAGTAAGATTATTTTGGTACACCTT  
TCTTGTAGTGTCTTATCAGTGAGTTGATTCATTTTCTACATTAATCAGT  
GTTTTCTGACCAGAAATATTGCTTGGATTTTTCTGAAAGTACAAAAAGCC  
ACATAGTTTTTTTTCAGAAAGGTTTCAAACCTCCTAAAGATTATTTCCAA  
GTATAAGTTTGTTTTTTATTTTCAATCTATGACTTGACTGGTATTAAAGCT  
GCTATTTGATAGTAATTAGATATATTCTCATTGATATAAACCTGTTTGGT  
TCAGCAAACAACTAAAATGATTGTACAGACAATGCTTTATTTTTCTG  
TTGGTGTGCTTGTGGGAAAAAGAAAGAGAGATCAGATTGTTACTGTGTC  
TGTGTAGAAAGAAGTAGACATAGGAGACTCCATTTTGTCTGTACTAAGA  
AAAATTCTTCTGCCTTGAGATGCTGTTAATCTATATAACCTTACCCCCAA  
CCCTGTGCTCTCTGAAACATGTGCTGTGTCCACTCAGGGTTAAATGGATT  
AAGGGCGGTGCAAGATGTGCTTTGTTAAACAGATGCTTGAAGGCAGCATG  
CTCGTAAGAGTCATCAACCTCCCTAATCTCAAGTACCCAGGGACACAAA  
CACTGCTGAAGGCGCAGGGACCTCTGCCTAGGAAAGCCAGGTATTGTCC  
AAGGTTTTCTCCCATGTGATAGTCTGAAATATGGCCTCGTGGGAGGGGAA  
AGACCTGACCGTCCCCAGCCGACACCCGTAAAGGGTCTGTGCTGAGGA  
GGATTAGTATACGAGGAAGGAACGCCTCTTGTGAGTTGAGACAAGAGGAA  
GGCATCTGTCTTCTGCCGTCCCTGGGCAATGGAATGTCTCGGTATAAAA  
CCCGATTTTATGTTCCATCTACTGAGATAGGGGAAAACACCTTAGGGCT  
GGAGGTGGGACATGCGGCAGCAATACTGCTCTTTAAGACATTGAGATGTT  
TATGTGTATGCATATCTAAAGCACAGCACTTAATTCTTTACCTTGTCTAT  
GTTGCAGAGACCTTTGTTACAGTGTATCTGCTGACCTTCTCTCCACTA  
TTATCCTATGACCCTGCCACATCCCCCTCTCCGAGAAACACCCAAGAATG  
ATCAATAAATACTAAGGGAACCTCAGAGGCCGGCGGGATCCTCCATATACT  
GAACGCTTGTCCCCTGGGCCCCCTTATTTCTTCTCTATACTGGTCTCT  
GTGCTTTTTTCTTTTCCAAGTCTCTCGTTCCACCTAATGAGAAACACCCA  
CAGGTGTAAAGGGGCAACCCACCCCTCATGTGCTGATTTGTGAGCGTGCT  
TTAAGGTGAAAAAGCATGAATGTAACTTCCTTAAAAAGGTACAGCATC  
CAATTCAAATATTTTTGTCTGATTTTAATGCTAGTTGATGTAGTGCTAT  
TAAAATTTTGTTCACATGGACACAGAGAGGGGAACAACACATACCAGGG  
CCTGTTGCGGGGTGGGGATGAGGGGAGGGAACTTAGAGGACAGGTGAACA  
GGTGACAGCATCACCATGGCCACATATACCTATTTAACAAACCTGCAC

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GTTCTGCACACGTATCCCATTTCTTTTTTTTTTTAAGAAATAGAAAAAA  
AATAAAATTTTGTTCACTGATTCTTCCATTTTAAACCTGTTTGCAATGTG  
GTTTAGGATGCCCTTACTTCAGCAAAGGAGAAGGAATAGGAGGGCCTTAG  
AATTTTGGAGGGAAAAAACCTATAACATACATTGTACTGTATCAAACCT  
ATTTTACATGAATGACACAAGTATTCTGAATAAAAAATAATTGAACATT  
GTTAAGAACAAGGTGTCATGTAATTTATTTTTCATAAATAAAAAATTAT  
AGTGGCTTAGACTGAAAGGAACAGAGAATTTAAAAAATTAAAAAGAAGCC  
TTAGTATATTTTGTATATAGTTTCCATGTGCCATATTTGCCATAATTGG  
ATGAGAATTTTGTACCTCTGGCAGGGTGACCCTATATTTTCANTNTATA  
AAGCGTGCATCATACC

MVLKCIIPPGIDSQCAIGVRVTALGHATQRVSSIXQIIPQI.WECIRKTEAWIIHPIII.I.NIISI.QPGGICSI.SNKCI.SSI.QRSASA  
I:KGSPII.I.GVSKQEFCL.YCDKDKGQSIIPSI.QI.KIEI.MKI.AAQKESARRPFIFYRAQVGSWNMLESA.AIIFGWIFCTSCNCF  
I:PVGIXNXVDIPII.I.GKAQKRGTYSE

FIG. 5

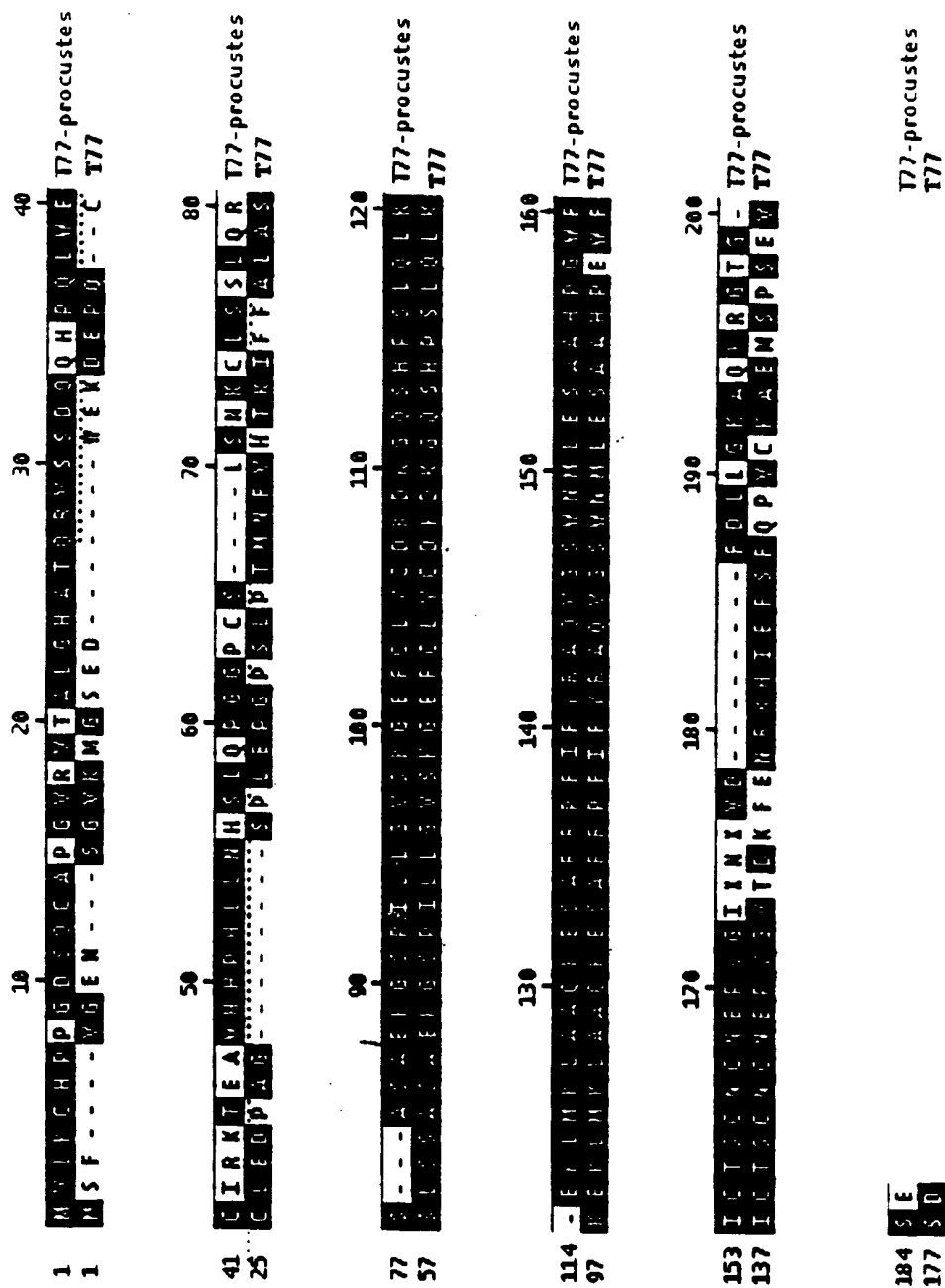


FIG. 6

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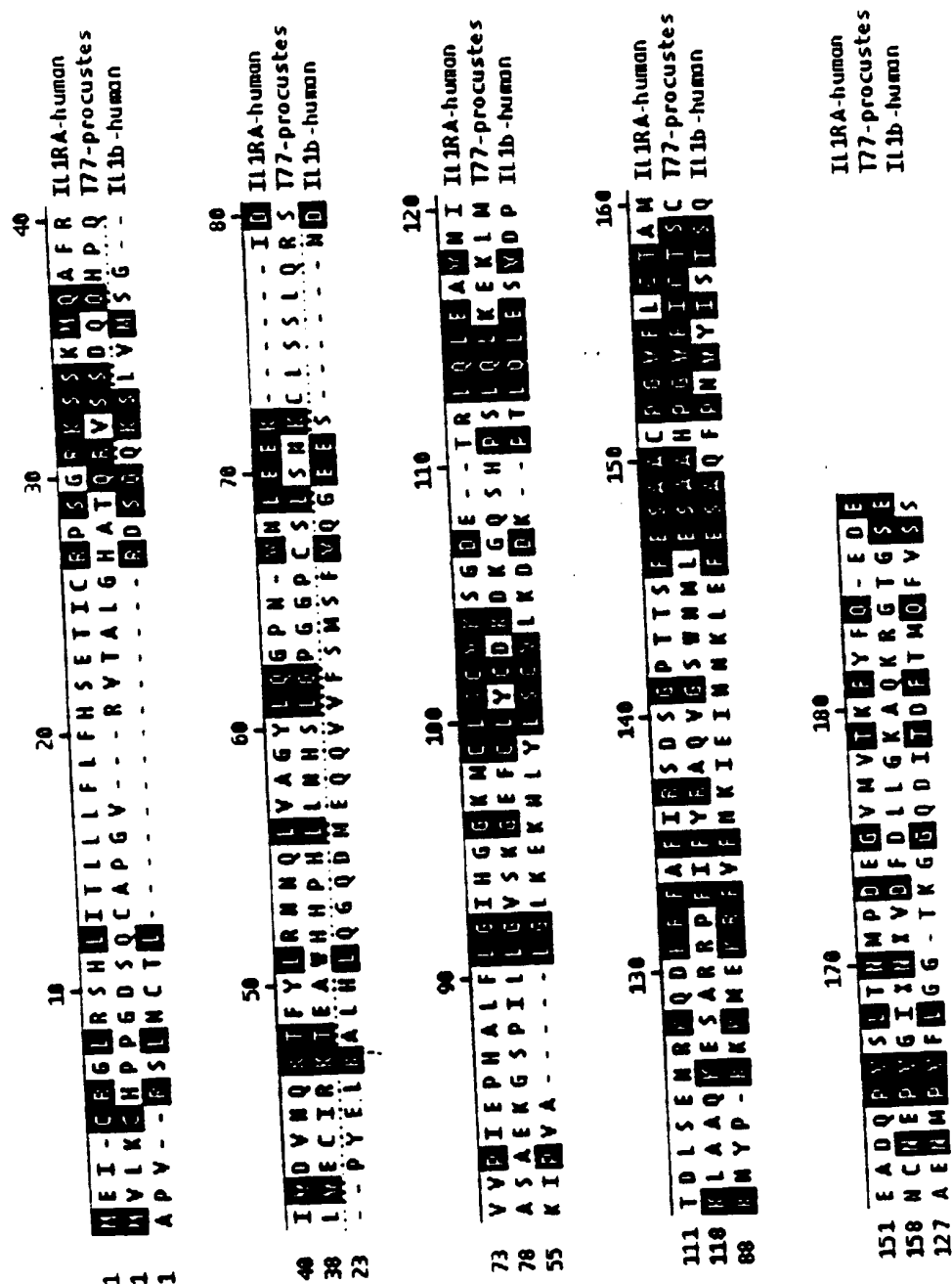


FIG. 7

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US98/16102

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) : C07H 21/02, 21/04, 1/00, 14/00, 17/00; C12Q 1/68; G01N 33/53  
US CL : 536/23.1; 530/350, 387.1; 435/6, 7.1

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 536/23.1; 530/350, 387.1; 435/6, 7.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
DIALOG: MEDLINE, USPATFUL, WPI, BIOSIS. Search terms include author, "TANGO" and protein

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	Database Medline on Dialog, US National Library of Medicine, (Bethesda, MD, USA) AN 09370320. SONNENFELD et al. 'The Drosophila tango gene encodes a bHLH-PAS protein that is orthologous to mammalian Arnt and controls CNS midline and tracheal development'. Development. November 1997, volume 124, number 22, pages 4571-82, Abstract.	1-22

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:	*T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
*A document defining the general state of the art which is not considered to be of particular relevance	*X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
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*L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	*A document member of the same patent family
*O document referring to an oral disclosure, use, exhibition or other means	
*P document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

21 OCTOBER 1998

Date of mailing of the international search report

30 OCT 1998

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